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(57) Abstract

A method for killing pests (e.g. insects) comprising administering material from *Xenorhabdus* species (e.g. *X. nematophilus*) such as cells or supernatants orally to the pests, either alone or in conjunction with *Bacillus thuringiensis* or pesticidal materials derived therefrom. Also disclosed is an isolated pesticidal agent (and compositions comprising the same) characterised in that it is obtainable from cultures of *X. nematophilus* or mutants thereof, has oral pesticidal activity against *Pieris brassicae*, *Pieris rapae* and *Plutella xylostella*, is substantially heat stable to 55 °C, is proteinaceous, acts synergistically with *B. thuringiensis* cells as an oral pesticide and is substantially resistant to proteolysis by trypsin and proteinase K. DNA encoding pesticidal activity is also disclosed.

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PESTICIDAL AGENTS

The present invention relates to materials, agents and compositions having pesticidal activity which derive from bacteria, and more particularly from *Xenorhabdus* species. The invention further relates to organisms and methods employing such compounds and compositions.

There is an ongoing requirement for materials, agents, compositions and organisms having pesticidal activity, for instance for use in crop protection or insect-mediated disease control. Novel materials are required to overcome the problem of resistence to existing pesticides. Ideally such materials are cheap to produce, stable, have a high toxicity (either when used alone or in combination) and are effective when taken orally by the pest target. Thus any invention which provided materials, agents, compositions or organisms in which any of these properties was enhanced would represent a step forward in the art.

Xenorhabdus spp. in nature are frequently symbiotically associated with a nematode host, and it is known that this association may be used to control pest activity. For instance, it is known that certain *Xenorhabdus spp.* alone are capable of killing an insect host when injected into the host's hemocoel.

In addition, one extracellular insecticidal toxin from *Photorhabdus luminescens* has been isolated (this species was recently removed from the genus *Xenorhabdus*, and is closely related to the species therein). This toxin is not effective when ingested, but is highly toxic when injected into certain insect larvae (see Parasites and Pathogens of Insects Vol.2, Eds. Beckage, N. E. et al., Academic Press 1993).

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Also known are certain low-molecular weight heterocyclic compounds from *P.luminescens* and *X.nematophilus* which have antibiotic properties when applied intravenously or topically (see Rhodes, S.H. et al., PCT WO 84/01775).

Unfortunately none of these prior art materials have the ideal pesticide characteristics discussed above, and in particular, they do not have toxic activity when administered orally.

The present invention provides pesticidal agents and compositions from *Xenorhabdus* species, organisms which produce such compounds and compositions, and methods which employ these agents, compositions and organisms, that alleviate some of the problems with the prior art.

According to one aspect of the present invention there is disclosed a method of killing or controlling insect pests comprising administering cells from *Xenorhabdus* species or pesticidal materials derived or obtainable therefrom, orally to the pests.

A PCT application of CSIRO published as WO 95/00647 discloses an apparently toxic protein from *Xenorhabdus nematophilus*; however no details of the protein's toxicity are given, and certainly there is no disclosure of its use as an oral insecticide.

Thus the invention provides an insecticidal composition adapted for oral administration to an insect, which composition comprises a pesticidal material obtainable from a *Xenorhabdus* species, or a pesticidal fragment thereof, or a pesticidal variant or derivative of either of these.

The composition may in fact comprise cells of *Xenorhabdus* or alternatively supernatant taken from cultur s of cells of *Xenorhabdus* species. However, the composition

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preferably comprises toxins isolable from *Xenorhabdus* as illustrated her inafter. Toxic activity has be n associated with material encoded by the nucleotide sequ nce of Figure 2. Thus, the composition suitably comprises a pesticidal material which is encoded by all or part of the nucleotide sequence of Figure 2. Pesticidal fragments as well as variants or derivatives of such toxins may also be employed.

The sequence of Figure 2 is of the order of 40kb in length. It is believed that this sequence may encode more than one protein, each of which may regulate or be insecticidal either alone or when presented together. It is a matter of routine to determine which parts are necessary or sufficient for insecticidal activity.

As used herein the term ``variant'' refers to toxins which have modified amino acid sequence but which share similar activity. Certain amino acids may be replaced with different amino acids without altering the nature of the activity in a significant way. The replacement may be by way of ``conservative substitution'' where an amino acid is replaced with an amino acid of broadly similar properties, or there may be some non-conservative substitutions. In general however, the variants will be at least 60% homologous to the native toxin, suitably at least 70% homologous and more preferably at least 90% homologous.

The term ``derivative'' relates to toxins which have been modified for example by chemical or biological methods.

These toxins are novel, and they and the nucleic acids which encode them form a further aspect of the invention.

A preferred *Xenorhabdus* species is the bacteria *X.nematophilus*. Particular strains of *X.nematophilus* which are us ful in the context of the inv ntion are

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ATTC 19061 strain, available from the National Collection of Industrial and Marine Bacteria, Aberdeen, Scotland (NCIMB). In addition, suitable strains include two novel strains of *Xenorhabdus* which were deposited at the NCIMB on 10 July 1997 and were designated with repository numbers NCIMB 40886 and NCIMB 40887. These latter strains form a further aspect of the invention.

All strains have common characteristics as set out in the following Table 1.

Table 1

	Strains		
Characteristics	ATCC 19061	NCIMB 40887	NCIMB 40886
Gram strain	negative	negative	negative
Shape/size	rods up to 4μm long	rods up to 4μm long	rods up to 4μm long
Motile	Yes	Yes	Yes
Bioluminescent	No	No	No
Colour on NBTA*	blue	blue	blue
insecticidal on ingestion by insects	yes	yes	yes
Production of Antibiotics	yes	yes	yes
Resistant to ampicillin (50μg/ml)	yes	yes	yes
colony morphology/ colour	circular convex cream	circular convex cream	circular convex cream

*NBTA (Oxoid nutrient agar containing 0.0025% bromothymol blue and 0.004% tetrazolium chloride)

Preferably the pest target is an insect, and more preferably it is of the order Lepidoptera, particularly

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Pieris brassicae, Pieris rapae, or *Plutella xylostella* or the order *Diptera,* particularly *Culex quinquefaciatus.*

In a preferred embodiment of the invention, cells from *Xenorhabdus* species or agents derived therefrom are used in conjunction with *Bacillus thuringiensis* as an oral pesticide.

In further embodiments, rather than using *Bacillus thuringiensis* itself, pesticidal materials obtainable from *B.thuringiensis* (e.g. delta endotoxins or other isolates) are used in conjunction with *Xenorhabdus* species.

The term 'obtainable from' is intended to embrace not only materials which have been isolated directly from the bacterium in question, but also those which have been subsequently cloned into and produced by other organisms.

Thus the unexpected discovery that bacteria of the genus *Xenorhabdus*(and materials derived therefrom) have pesticidal activity when ingested, and that such bacteria and materials can be used advantageously in conjunction with *B.thuringiensis* (and toxins or materials derived therefrom), forms the basis of a further aspect of the present invention. The pesticidal activity of *B.thuringiensis* isolates alone have been well documented. However, synergistic pesticidal activity between such isolates and bacteria of the *Xenorhabdus* species (or materials derived therefrom) has not previously been demonstrated.

In still further embodiments of the invention, culture supernatant taken from cultures of *Xenorhabdus* species, particularly *X. nematophilus*, is used in place of cells from *Xenorhabdus* species in the methods above.

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All of these methods can be employed, inter alia, in pest control.

The invention also makes available pesticidal compositions comprising cells from *Xenorhabdus* species, preferably *X.nematophilus*, in combination with *B. thuringiensis*. As with the methods above, a pesticidal toxin from *B.thuringiensis* (preferably a delta endotoxin) may be used as an alternative to *B.thuringiensis* in the compositions of the present invention

Likewise, culture supernatant taken from cultures of *Xenorhabdus* species, preferably, *X.nematophilus* may be used in place of cells from *Xenorhabdus* species.

Such compositions can be employed, *inter alia*, for crop protection eg. by spraying crops, or for livestock protection. In addition, compositions of the invention may be used in vector control.

The invention further encompasses novel pesticidal agents which can be isolated from *Xenorhabdus spp*. Techniques for isolating such agents would be understood by the skilled person.

In particular, such techniques include the separation and identification of toxin proteins either at the protein level or at the DNA level.

The applicants have cloned and partially sequenced a region of DNA from *Xenorhabdus* NCIMB 40887 which region codes for insecticidal activity and this is shown as Figure 2 (SEQ ID NO. 1) hereinafter. Thus in a preferred embodiment the invention also provides a toxin which is encoded by DNA of SEQ ID No. 1 or a variant or fragment thereof.

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The invention also provides a recombinant DNA which encodes such a toxin. The recombinant DNA of the invention may comprise the sequence of Figure 2 or a variant or fragment thereof. Other DNA sequences may encode similar proteins as a result of the degeneracy of the genetic code. All such sequences are encompassed by the invention.

The sequence provided herein is sufficient to allow probes to be produced which can be used to identify and subsequently to extract DNA of toxin genes. This DNA may then be cloned into vectors and host cells as is understood in the art.

DNA which comprises or hybridises with the sequence of Figure 2 under stringent conditions forms a further aspect of the invention.

The expression ``hybridises with'' means that the nucleotide sequence will anneal to all or part of the sequence of Figure 2 under stringent hybridisation conditions, for example those illustrated in ``Molecular Cloning'', A Laboratory Manual'' by Sambrook, Fritsch and Maniatis, Cold Spring Habor Laboratory Press, Cold Spring Harbor, N.Y.

The length of the sequence used in any particular analytical technique will depend upon the nature of the technique, the degree of complementarity of the sequence, the nature of the sequence and particularly the GC content of the probe or primer and the particular hybridisation conditions employed. Under high stringency, only sequences which are completely complementary will bind but under low stringency conditions, sequences which are 60% homologous to the target sequence, more suitably 80% homologous, will bind. Both high and low stringency conditions are encompassed by the term ``stringent conditions'' used herein.

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Suitable fragments of the DNA of Figure 2, i.e. those which encode pesticidal agents may be identified using standard techniques. For example, transposon mutagenesis techniques may be used, for example as described by H.S. Siefert et al., Proc. Natl. Acad. Sci. USA, (1986) 83, 735-739. Vectors such as the cosmid cHRIMI, can be mutated using a variety of transposons and then screened for loss of insectidal activity. In this way regions of DNA encoding proteins responsible for toxic activity can be identified.

For example, the mini-transposon mTn3(HIS3) can be introduced into a toxic *Xenorhabdus* clone such as cHRIM1, hereinafter referred to as `clone 1', by electroporating cHRIM1 DNA into *E.coli* RDP146(pLB101) and mating this strain with *E.coli* RDP146(pOX38), followed by *E. coli* NS2114Sm. The final strain will contain cHRIM1DNA with a single insertion of the transposon mTn3(HIS3). These colonies can be cultured and tested for insecticidal activity as described in Example 8 hereinafter. Restriction mapping or DNA sequencing can be used to identify the insertion point of mTn3(HIS3) and hence the regions of DNA involved in toxicity. Similar approached can be used with other transposons such as Tn5 and mTn5.

Site directed mutagenesis of cHRIM1 as outlined in ``Molecular Cloning, A Laboratory Manual'' by Maniatis, Fritsch and Sambrook, (1982) Cold Spring Harbor, can also be used to test the importance of specific regions of DNA for toxic activity.

Alternatively, subcloning techniques can be used to identify regions of the cloned DNA which code for insecticidal activity. In this method, specific smaller fragments of the DNA are subcloned and the activity determin d. To do this, cosmid DNA can be cut with a suitable restriction enzyme and ligated into a compatible

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restriction site on a plasmid vector, such as pUC19. The ligation mix can be transformed into *E. coli* and transformed clones selected using a selection marker such as antibiotic resistance, which is coded for on the plasmid vector. Details of these techniques are described for example in Maniatis et al, supra, (see p390-391) and Methods in Molecular Biology, by L.G. Davies, M.D. Dibner and J.F. Battey, Elsevier, (see p222-224).

Individual colonies containing specific cloned fragments can be cultured and tested for activity as described in Example 8 hereinafter. Subclones with insecticidal activity can be further truncated using the same methodology to further identify regions of the DNA coding for activity.

The invention also discloses an isolated pesticidal agent characterised in that the agent is obtainable from cultures of *X. nematophilus* or variants thereof, has oral pesticidal activity against *Pieris brassicae, Pieris rapae* and *Plutella xylostella*, is substantially heat stable to 55°C, is proteinaceous, acts synergistically with *B.thuringiensis* cells as an oral pesticide and is substantially resistant to proteolysis by trypsin and proteinase K.

By 'substantially heat stable to 55°C' is meant that the agent retains some pesticidal activity when tested after heating the agent in suspension to 55°C for 10 minutes, and preferably retains at least 50% of the untreated activity.

By 'substantially resistant to proteolysis' is meant that the agent retains some pesticidal activity when exposed to proteases at 30°C for 2 hours and preferably retains at least 50% of the untreated activity.

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By 'acts synergistically' is meant that the activity of the combination of compon nts is greater than one might expect from the use of the components individually. For example, when used in conjunction with *B.thuringiensis* cells as an oral pesticide, the concentration of B. thuringiensis cellular material necessary to give 50% mortality in a P.brassicae when used alone is reduced by at least 80% when it is used in combination the agent at a concentration sufficient to give 25% mortality when the agent is used alone.

It has been found that the activity of the material is retained by 30 kDa cut-off filters but is only partly retained by 100 kDa filters.

Preferably the agent is still further characterised in that the pesticidal activity is lost through treatment at 25°C with sodium dodecyl sulphate (SDS - 0.1% 60 mins) and acetone (50%, 60 mins).

Clearly the characterising properties of the isolated agent described above can be utilised to purify it from, or enrich its concentration in, *Xenorhabdus* species cells and culture medium supernatants. Methods of purifying proteins from heterogenous mixtures are well known in the art (eg. ammonium sulphate precipitation, proteolysis, ultrafiltration with known molecular weight cut-off filters, ion-exchange chromatography, gel filtration, etc.). The oral pesticidal activity provides a convenient method of assaying the level of agent after each stage, or in each sample of eluent. Such methodology does not require inventive endeavour by those skilled in the art.

The invention further discloses oral pesticidal compositions comprising one or more agents as described above. Such compositions preferably further comprise other pesticidal materials from non-*Xenorhabdus* species.

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These other materials may be chosen such as to have complementary properties to the agents described abov , or act synergistically with it.

Preferably the oral pesticidal composition comprises one or more pesticidal agents as described above in combination with *B. thuringiensis* (or with a toxin derived therefrom, preferably endotoxin).

Recombinant DNA encoding said proteins also forms a further aspect of the invention. The DNA may be incorporated into an expression vector under the influence of suitable control elements such as promoters, enhancers, signal sequences etc. as is understood in the art. These expression vectors form a further aspect of the invention. They may be used to transform a host organism so as to ensure that the organism produces the toxin.

The invention further makes available a host organism comprising a nucleotide sequence coding for a pesticial agent as described above.

Methods of cloning the sequence for a characterised protein into a host organism are well known in the art. For instance the protein may be purified and sequenced: as activity is not required for sequencing, SDS gel electrophoresis followed by blotting of the gel may be used to purify the protein. The protein sequence can be used to generate a nucleotide probe which can itself be used to identify suitable genomic fragments from a *Xenorhabdus* gene library. These fragments can then be inserted via a suitable vector into a host organism which can express the protein. The use of such general methodology is routine and non-inventive to those skilled in the art. Such techniques may be applied to the production of *X norhabdus* toxins other than those encoded by the sequence of Figure 2.

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It may be desirable to manipulate (eg. mutate) the agent by altering its gene sequence (and hence protein structure) such as to optimise its physical or toxicological properties.

It may also be desirable for the host to be engineered or selected such that it also expresses other proteinaceous pesticidal materials (eg. delta- endotoxin from *B. thuringiensis*). Equally it may be desirable to generate host organisms which express fusion proteins composed of the active portion of the agent plus these other toxicity enhancing materials.

A host may be selected for the purposes of generating large quantities of pesticidal materials for purification e.g. by using *B.thuringiensis* transformed with the agent-coding gene. Preferably however the host is a plant, which would thereby gain improved pest-resistance. Suitable plant vectors, eg. the Ti plasmid from *Agrobacterium tumefaciens*, are well known in the art. Alternatively the host may be selected such as to be directly pathogenic to pests, eg. an insect baculovirus.

The teaching and scope of the present invention embraces all of these host organisms plus the agents, mutated agents or agent-fusion materials which they express.

Thus the invention makes available methods, compositions, agents and organisms having industrially applicable pesticidal activity, being particularly suited to improved crop protection or insect-mediated disease control.

The methods, compositions and agents of the present invention will now be described, by way of illustration only, through reference to the following non-limiting examples and figures. Other embodiments falling within

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the scope of the invention will occur to those skilled in the art in the light of these.

FIGURE

Figure 1 shows the variation with time of the growth of *X. nematophilus* ATCC 19061 and activity of cells and supernatants against *P. brassicae* as described in Example 3.

Figure 2 shows the sequence of a major part of a cloned toxin gene from *Xenorhabdus*.

Figure 3 shows a comparison of the restriction maps of cloned toxin genes from two strains of *Xenorhabdus* (clone 1 above and clone 3 below).

EXAMPLES

Example 1 - Use of *X. nematophilus* cells as an oral insecticide

CELL GROWTH: A subculture of *X.nematophilus* (ATCC 19061, Strain 9965 available from the National Collections of Industrial and Marine Bacteria, Aberdeen, Scotland) was used to inoculate 250 ml Erlenmeyer flasks each containing 50 ml of Luria Broth containing 10g tryptone, 5g yeast extract and 5g NaCl per litre. Cultures were grown in the flasks at 27°C for 40hrs on a rotary shaker.

PRODUCTION OF CELL SUSPENSION: Cultures were centrifuged at 5000 x *g* for 10 mins. The supernatants were discarded and the cell pellets washed once and resuspended in an equal volume of phosphate buffered saline (8g NaCl, 1.44g Na_2HPO_4 and 0.24g of KH_2PO_4 per litre) at pH 7.4.

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ACTIVITY OF CELL SUSPENSION TO INSECTS: The bioassays were as follows: *P. brassicae*: The larvae were allowed to feed on an artificial agar-based diet (as described by David and Gardiner (1965) London Nature, 207, 882-883) into which a series of dilutions of cell suspension had been incorporated. The bioassays were performed using a series of 5 doses with a minimum of 25 larvae per dose. Untreated and heat-treated (55°C for 10 minutes) cells were tested. Mortality was recorded after 2 and 4 days with the temperature maintained at 25°C.

	LC50 cells/g diet	
Treatment	2 days	4 days
Untreated	5.9×10^5	9.8×10^4
Treated 55°C	7.1×10^5	1.4×10^5

Aedes aegypti: The larva were exposed to a series of 5 different dilutions of cell suspension in deionised water. The biosassays were performed using 2 doses per dilution of 50 ml cell suspension in 9.5cm plastic cups with 25 second instar larvae per dose. Untreated and heat-treated (55°C or 80°C for 10 minutes) cells were tested. Mortality was recorded after 2 days with the temperature maintained at 25°C.

	LC50 cells/ml
Treatment	2 days
Untreated	5.1×10^6
Treated 55°C	7.4×10^6
Treated 80°C	$> 10^8$

Culex quinquefaciatus: The larvae were exposed to a single concentration cell suspension containing 4 $\times 10^7$ cells/ml. The biosassays were performed using 2 50 ml cell suspensions in 9.5 cm plastic cups with 25 second instar larvae per cup. Untreated and heat-treated (55°C or 80°C for 10 minutes) cells were tested. Mortality was

recorded after 2 days with the temperature maintained at 25°C.

Treatment	% Mortality 2 days
Untreated	100
Treated 55°C	100
Treated 80°C	0

Thus these results clearly show that cells from *X. nematophilus* are effective as an oral insecticide against a number of insect species (and are particularly potent against *P.brassicae*). The insecticidal activity is not dependent on cell viability (i.e is largely unaffected by heating to 55°C which reduces cell viability by >99.99%) but is much reduced by heating to 80°C, which denatures most proteins.

Example 2 - Use of *X.nematophilus* supernatant as an oral insecticide

CELL GROWTH: Cultures were grown as in Example 1.

PRODUCTION OF SUPERNATANT: Cultures were centrifuged twice at 10000g for 10 mins. The cell pellets were discarded.

ACTIVITY OF SUPERNATANT TO INSECTS: The Bioassay was as follows:
Activity against neonate *P. brassicae* and two day old *Pieris rapae* and *Plutella xylostella* larvae was measured as for *P. brassicae* in Example 1, but using a series of untreated dilutions of supernatant in place of of cell supensions and with mortality being recorded after 4 days only.

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Insect species	LC50 (μl supernatant/g diet) 4 days
P. brassicae	22
P. rapae	79
P. xylostella	135

In addition, size-reducing activity (62% reduction in 7 days) against *Mamestra brassicae* was detected in larvae fed on an artificial diet containing *X. nematophilus* supernatant (results not shown).

Thus these results clearly show that the supernatant from *X. nematophilus* culture medium is effective as an oral insecticide against a number of insect species, and are particularly potent against *P. brassicae*.

The heating of supernatants to 55°C for 10 minutes caused a partial loss of activity while 80°C caused complete loss of activity. Activity was also completely lost by treatment with SDS (0.1%w/v for 60 mins) and Acetone (50% v/v for 60 mins) but was unaffected by Triton X-100 (0.1% 60 mins), non-diet P40 (0.1% 60 mins), NaCl (1 M for 60 mins) or cold storage at 4°C or -20°C for 2 weeks. All of these properties are consistent with a proteinaceous agent.

The general mode of action of *X. nematophilus* cells and supernatants i.e. reduction in larval size and death within 2 days at high dosages, and other properties, eg. temperature resistence, appear to be similar suggesting a single agent or type of agent may be responsible for the oral insecticide activity activities of both cells and supernatants.

Example 3 - Timescale for appearance of ingestable ins cticidal activity

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CELL GROWTH: 1ml of an overnight culture of *X. nematophilus* was used to inoculate an Erlenmeyer flask. Cells were then cultured as in Example 1. Growth was estimated by measuring the optical density at 600 nm.

PRODUCTION OF CELL SUSPENSION AND SUPERNATANTS: These were produced as in Examples 1 and 2.

ACTIVITY OF CELLS AND SUPERNATANTS AGAINST *P. BRASSICAE*: The cell suspension bioassay was carried out as in Example 1, but using a single dose of suspended cells equivalent to 50 μl of broth/g diet and measuring mortality after 2 days. The cell supernatant bioassay was carried out as in Example 2, but using a single dose equivalent to 50 μl supernatant/g diet (i.e. more than twice the LC50) and measuring mortality after 2 days.

The results are shown in Fig. 1. Thus these results clearly show that cells taken from *X. nematophilus* culture medium are highly effective as an oral insecticide against *P. brassicae* after only 5 hours, and supernatants are highly effective after 20 hours. Although some slight cell lysis was observed in the early stages of growth, no significant cell lysis was observed after this point demonstrating that the supernatant activity may be due to an authentic extracellular agent (as opposed to one released only after cell breakdown).

Example 4 - Synergy between *X. nematophilus* cells and *B.thuringiensis* powder preparations

CELL GROWTH AND SUSPENSION: *X. nematophilus* cells were grown and suspended as in Example 1. *B. thuringiensis* strain HD1 (from *Bacillus* Genetic Stock Centre, The Ohio State University, Columbus, Ohio 43210, USA) was cultured, harvested and formulated into a powder as described by Dulmage *et al.*(1970) J. Invertebrate Pathology 15, 15-20.

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ACTIVITY OF *X. NEMATOPHILUS* CELLS AND *B. THURINGIENSIS* POWDER AGAINST *P. BRASSICAE*: The bioassays was carried out using *X. nematophilus* and *B. thuringiensis* in combination or using *B. thuringiensis* cell powder alone. Bioassays were carried out as in Example 1 but with various dilutions of *B. thuringiensis* powder in place of *X. nematophilus*. For the combination experiment, a constant dose of *X. nematophilus* cell suspension sufficient to give 25% mortaility was also added to the diet. Mortality was recorded after 2 days.

Bioassay	LC50 (μg Bt powder/g diet) 2 days
B.t. alone	1.7
B.t. plus *X.nematophilus*	0.09

These results clearly demonstrate the synergism between *X. nematophilus* cells and *B. thuringiensis* powder when acting as an oral insecticide against *P. brassicae*.

Example 5 - Synergy between of *X.nematophilus* supernatants and *B. thuringiensis* powder

CELL GROWTH AND PRODUCTION OF SUPERNATANTS: *X. nematophilus* cells were grown and supernatants prepared as in Example 2. *B. thuringiensis* was grown and treated as in Example 4.

ACTIVITY OF *X. NEMATOPHILUS* SUPERNATANTS AND Bt CELL POWDER AGAINST *P. BRASSICAE*:
The bioassays were carried out using *X. nematophilus* supernatants and *B. thuringiensis* in combination or using *B. thuringiensis* powder alone. The Bioassay against neonate *P. brassicae* and two day old *Pieris rapae* and *Plutella xylost lla* larvae w re measured as in Example 2 but with various dilutions of *B. thuringiensis* in place of *X. nematophilus*. For the combination experiment, a

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constant dose of *X. nematophilus* supernatant sufficient to give 25% mortality was also added to the diet. Mortality was recorded after 4 days.

	LC_{50} (µg Bt powder/g) diet	
Insect species	Bt alone	Bt plus Xn
P. brassicae	1.4	0.12
P. rapae	2.5	0.26
P. xylostella	7.2	0.63

These results clearly demonstrate the synergism between *X.nematophilus* supernatants and *B.thuringiensis* powder when acting as an oral insecticide against several insect species. The fact that both *X. nematophilus* cells and supernatants demonstrate this synergism strongly suggests that a single agent or type of agent is responsible for the demonstrated activities.

Example 5 - Characterisation of insecticidal agent from *X.nematophilus* supernatant by proteolysis

CELL GROWTH AND PRODUCTION OF SUPERNATANTS: *X. nematophilus* cells were grown and supernatants prepared as in Example 2.

PROTEOLYSIS OF SUPERNATANT: Culture supernatant (50ml) was dialysed against 0.5 M NaCl (3 x 1 l) for 48 hours at 4°C. The volume of the supernatant in the dialysis tube was reduced five-fold by covering with polyethylene glycol 8000 (Sigma chemicals). Samples were removed and treated with either trypsin (Sigma T8253 = 10,000 units/mg) or proteinase K (Sigma P0390 = 10 units/mg) at a concentration of 0.1 mg protease/ml sample for 2 hours at 30°C.

ACTIVITY OF PROTEASE TREATED SUPERNATANT AGAINST *P. BRASSICAE*: The boassay against neonate *P. brassicae*

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larvae was carried out by spreading 25 μl of each 'treatment' on the artificial agar-based diet referred to in Example 1 in a 4.5 cm diameter plastic pot. Four pots each containing 10 larvae were used for each treatment. Mortalities were recorded after 1 and 2 days. Controls using water only, trypsin (0.1 mg/ml) and proteinase K (0.1 mg/ml) were also tested in the same way.

	% Mortality	
Treatment	1 day	2 days
Untreated supernatant	60	100
Proteinase K treated supernatant	45	100
Trypsin treated supernatant	40	100
All controls (no supernatant)	0	0

Example 6

Entomocidal activity of other *Xenorhabdus*

Using the methodology of Examples 1 and 2, four different *xenorhabdus* strains were tested against insect pests. The results obtained were as follows:

I) Activity to *Pieris brassicae*

Strain deposit no/code	Cells 10^6/grm diet % mortality	Supernatant LC50 μl/gram of diet
NCIMB 40887	100	0.09
0014	100	0.52
0015	80	3.73
NCIMB 40886	100	0.05

It was found that entomocidal activity of cells and supernatant was reduced by more than 99% when all four strains were heated at 80°C for 10 minutes.

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II) Activity to mosquitoes (*Aedes aegypti*)
Bacteria added at the rate of 10^7cells/ml of water

Strain deposit no/code	Cells 10^6/grm diet % mortality
NCIMB 40887	0
0014	40
0015	45
NCIMB 40886	95

Furthermore, all strains significantly reduced the growth of *Heliothis virescens*.

Example 7

Cloning of toxin genes from strains of *Xenorhabdus*

Total cellular DNA was isolated from NCIMB 40887 and ATCC 19061 using a Quiagen genomic purification DNA kit. Cells were grown in L borth (10g tryptone, 5g yeast extract and 5g NaCl per l) at 28°C with shaking (150rpm) to an optical density of 1.5 A_{600}. Cultures were harvested by centrifugation at 4000xg and resuspended in 3.5mls of buffer B1 (50mM Tris/HCl, 0.05% Tween 20, 0.5% Triton X-100, pH7.0) and incubated for 30 mins at 50°C. DNA was isolated from bacterial lysates using Quiagen 100/G tips as per manufacturers instructions. The resulting purified DNA was stored at -20°C in TE buffer (10mM Tris, 1mM EDTA, pH 8.0).

A representative DNA library was produced using total DNA of NCIMB 40887 and ATTC 19061 partially digested with the restriction enzyme *Sau3a*. Approximately 20µg of DNA from each strain was incubated at 37°C with 0.25 units of the enzyme. At time intervals of 10, 20, 30, 45 and 60 minutes, samples were withdrawn and heated at 65°C for 15 minutes. To visualise the size of the DNA fragments, the samples were electrophoresed on 0.5% w/v agarose gels.

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The DNA samples which contained the highest proportion of 30 to 50kb fragments were combined and treated with 4 units of shrimp alkaline phosphatase (Boehringer) for 15 minutes at 37°C, followed by heat treatment at 65°C to inactivate the phosphatase.

The size selected DNA fragments were ligated into the BamH1 site of the cosmid vector SuperCos! (Stratagent) and packaged into the *Escherichia coli* strain XL Blue 1, using a Gigapack II packaging kit (Stratgene) in accordance with the manufacturers instructions.

To select for cosmid clones with entomocidal activity, individual colonies selected on L agar plates containing 25μg/ml ampicillin, were grown in L broth (containing 25μg/ml ampicillin) overnight at 28°C. Broth cultures (50μl) were individually spread onto the surface of insect diet contained in 4.5cm diameter pots, as described in Example 5. To each container 10 neonate *P. brassicae* larvae were added. Larvae were examined after 24, 72 and 96 hours recording mortality and size of surviving larvae. A total of 220 clones of NCIMB 40887 were tested, of which two were found to cause reduction in larval growth and death within 72 hours. Of 370 clones from ATTC 19061, one was found to cause larval death within 72 hours.

Example 8

<u>Activity of cloned toxin genes to *Pieris brassicae*</u>

The three active clones from Example 7 were grown in L broth, containing 25μg/ml ampicillin, for 24 hours at 28°C, on a rotary shaker at 150rpm. The activity of the toxin clones to neonate larvae were performed by incorporation of whole broth cultures into insect diet, as described in Example 1.

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Clone No	Strain	LC50 (µl broth/g insect diet)
1	NCIMB 40887	13.03
2	NCIMB 40887	16.7
3	ATTC 19061	108.7
Control*		No effect at 100µl/g

*XL1 Blue *E. coli* broth

When *E. coli* toxin clones were heated at 80°C for 10 minutes and added to the diet at a rate of 100µl/g, no activity to larvae was detected. Highlighting the heat sensitivity of the toxins.

Example 9

Sequencing of the cloned toxin from NCIMB 40887

Cosmid DNA of the entomocidal clone 1 above from NCIMB 40887 was purified using the Wizard Plus SV DNA system (Promega) in accordance with the manufacturers instructions. A partial map of the cloned fragment was obtained using a range of restriction enzymes *Eco*R1, *Bam*H1, *Hind*III, *Sal*1 and *Sac*1 as shown in Figure 3. DNA sequencing was intiatiated from pUC18 and pUC19 based sub-clones of the cosmid, using the enzymes *Eco*R1, *Bam*H1, *Hind*III, *Eco*RV and *Pvu*II. Sequence gaps were filled using a primer walking approach on purified cosmid DNA. Sequence reactions were performed using the ABI PRISM™ Dye Terminator Cycle Sequencing Ready Reaction Kit with AmmpliTaq DNA polymerase FS according to the manufacturers instructions. The samples were analysed on an ABI automated sequencer according to the manufacturers instructions. The major part of the DNA sequence for the cloned toxin fragment is shown in Figure 2.

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Example 10

<u>Restriction map of cloned toxin from clone 3</u>

Cosmid DNA of the entomocidal clone 3 above was purified as described in Example 9. A restriction map of the cloned fragment was obtained using the restriction enzymes *Bam*H1, *Hind*III, *Sal*1 and *Sac*1 and this is shown in Figure 3. When compared with the map from clone 1 (Figure 3) it is clear that over the regions which overlap, the restriction maps are very similar. The only detectable difference between the two clones was a reduction in size of two *Hind*III fragments in clone 3, corresponding to the 11.4kb and 7.2kb *Hind*III fragments in clone 1 by approximately 2Kb and 200bp respectively. These results indicate the overall relatedness of the DNA region coding for toxicity in the two bacterial strains.

Example 11

<u>Southern Blot Hybridisation Experiments</u>

A 10.3kb *Bam*H1-*Sal*1 fragment of the DNA from clone 1 was used as a probe to hybidise to total *Hind*III digested DNA of the *Xenorhabdus* strains ATCC 19061, NCIMB 40886 and NCIMB 40887. Hybridisation was performed with 20ng/ml of DIG labelled DNA probe at 65°C for 18 hours. Filters were washed prior to immunological detection twice for 5 minutes with 2 x SSC (0.3M NaCl, 30mM sodium citrate, pH 7.0)/0.1% (w/v) sodium dodecyl sulphate at room temperature, and twice for 15 minutes with 0.1 x SSC (15mM NaClm 1.5 mM sodium citrate, pH 7.0) plus 0.1% sodium dodecyl sulphate at 65°C. The probe was labelled and experiments performed in accordance with manufacturers instructions, using a non-radioactive DIG DNA labelling and detection kit (Boehringer). The probe hybridised to a *Hind*III fragment of approximately 8kb in all three strains as well as an 11.4kb fragment in NCIMB 40887 and an approximate 9kb fragment in both NCIMB 40886 and ATCC 19061. These results show that strains NCIMB

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40886 and ATCC 19061 contain DNA with close homology to the toxin gene of clone 1 above, confirming the similarity between the toxins produced by the three strains.

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CLAIMS

1. An insecticidal composition adapted for oral administration to an insect comprising a pesticidal material obtainable from a *Xenorhabdus* species, or a pesticidal fragment thereof, or a pesticidal variant or derivative of either of these.

2. A composition according to claim 1 wherein the said pesticidal material comprises material encoded by the nucleotide sequence of Figure 2 or variant or fragment thereof, or a sequence which hybridises with said sequence.

3. A composition according to claim 1 or claim 2 which comprises cells of *Xenorhabdus*.

4. A composition as claimed in any one of the preceding claims which comprises supernatant taken from cultures of cells of *Xenorhabdus* species.

5. A composition according to any one of the preceding claims wherein the *Xenorhabdus* species is *Xenorhabdus nematophilus*.

6. A composition according to any one of claims 1 to 4 wherein the *Xenorhabdus* species is ATCC 19061, NCIMB 40886 or NCIMB 40887.

7. A composition as claimed in any one of the preceding claims which comprises a further pesticidal material not obtainable from *Xenorhabdus*.

8. A composition according to claim 7 wherein the said further pesticidal material comprises a material obtainable from *B. thuringiensis*.

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9. A composition according to claim 8 which further comprises cells of *B. thuringiensis*.

10. A composition according to claim 8 wherein the pesticidal materials obtainable from *B.thuringiensis* comprises the delta endotoxin.

11. A composition according to any one of the preceding claims which further comprises an agriculturally acceptable carrier.

12. A composition according to claim 10 wherein the carrier comprises items of insect diet.

13. A method for killing or controlling insect pests, which method comprises administering to a pest or the environment thereof a composition according to any one of the preceding claims.

14. A method as claimed in claim 12 wherein the pests are insects from the order Lepidoptera or Diptera.

15. A microorganism comprising *Xenorhabdus* strain NCIMB 40886.

16. A microorganism comprising *Xenorhabdus* strain NCIMB 40887.

17. A pesticidal agent which comprises a a toxin comprising a protein which is encoded by DNA which includes SEQ ID No. 1 or a variant or fragment thereof.

18. An isolated pesticidal agent characterised in that it is obtainable from cultures of *X. nematophilus* or mutants thereof, has oral pesticidal activity against *Pieris brassicae*, *Pieris rapae* and *Plutella xylostella*, is substantially heat stabl to 55°C, is proteinaceous, acts synergistically with *B. thuringiensis* cells as an

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oral pesticide, and is substantially resistant to proteolysis by trypsin and proteinase K.

19. An isolated pesticidal agent as claimed in claim 18 further characterised in that the pesticidal activity is substantially destroyed by treatment with sodium dodecyl sulphate or acetone or heating to 80°C.

20. An isolated pesticidal agent as claimed in claim 18 or claim 19 further characterised in that the agent is an extracellular protein.

21. A recombinant DNA which encodes a pesticidal agent according to any one of claims 17 to 20.

22. A recombinant DNA of claim 21 which comprises the sequence of Figure 2 or a variant or fragment thereof.

23. A recombinant DNA which comprises or hybridises under stringent conditions with all or part of the sequence of Figure 2, and which encodes a pesticidal material.

24. An expression vector comprising a recombinant DNA according to any one of claims 21 to 23.

25. A host organism which has been transformed with an expression vector according to claim 24.

26. A host organism as claimed in claim 25 which has been engineered or selected such that it also expresses other pesticidal proteinaceous toxicity enhancing materials

27. A host organism comprising a nucleotide sequence coding for a fusion protein comprising a pesticidally active portion of an agent as claimed in any one of claims 17 to 20 in combination with other pesticidal proteinaceous toxicity enhancing materials.

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28. A host organism as claimed in claim 27 wherein the pesticidal toxicity enhancing materials comprise delta-endotoxin from B. thuringiensis.

29. A host organism as claimed in any one of claims 25 to 289 wherein the host is a plant.

30. A host organism as claimed in any one of claims 25 to 28 wherein the host is a virus pathogenic to insects.

31. A fusion protein as expressed by a host as claimed in claim 27.

32. An pesticidal composition comprising one or more agents as claimed in any one of claims 17 to 20.

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Fig.1.

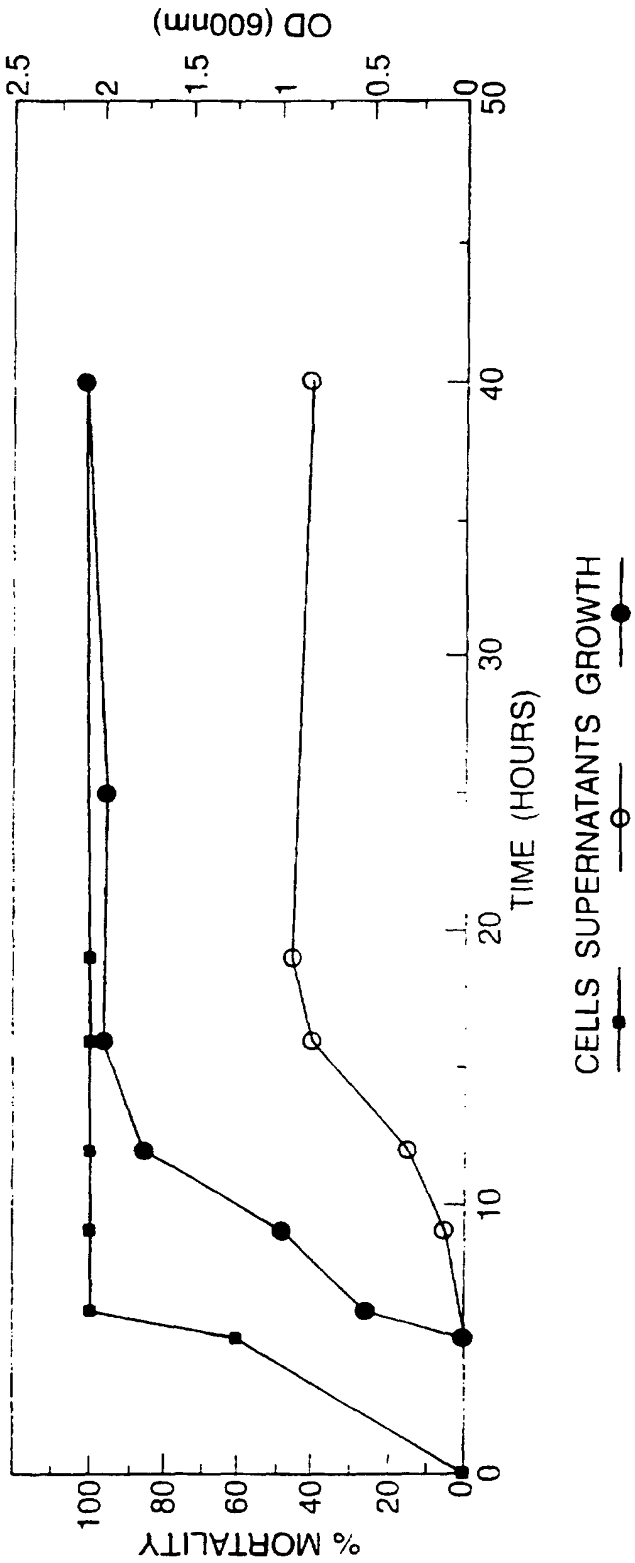

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Fig.2.

1	TCCACAATTG	CCGGAGAAAA	TCAGTCGGGA	ACTGCCGGTG	ATTATTCGTC	ACTTATTAAA
61	CGAATTTGCC	GACCAGAATA	AGGCTAAAAA	ACTGCTACAG	GCGCAACGCG	ACTCGAACGA
121	AGCGTTAACG	GTAAAGAGTC	ATTCGGATCC	GCTGTATCGC	TTTTGTGGTT	ATCTGGTGTC
181	TGTCAATGAT	ATGACCGGAA	TGAAGATGGG	CAATAAAAAC	ATTAGCCCAC	GAGCACCGAG
241	ATTGTACTTG	TATCATGCCT	ATCTCTCTTT	TATGGAAGCG	CACGGCTTTG	AACGTCCGTT
301	AACACTGACT	AAGTTTGGTG	AATCCATCCC	CAAGATTATG	CTGGAATACC	GGAAGGAGTA
361	TCGAAAAGTG	CGAACCAAGA	AAGGCTATTC	CTATAACGTG	GAATTATCGG	AAGAGGCCGA
421	AGAATGGCTA	CCGTCAGTGC	CTGAGTGTCG	AGACTTTAAA	TCACCTGTAT	AAAACTTTGA
481	GCTTTAAGTC	TGCACTCCAT	ACACAACTTA	AAATATCTAA	TTGTATTTAA	AAGAAAATAA
541	TAGATGTATA	GTTATTTTTT	AACTATACAT	AAGCTCTACA	TGCTCTTCAT	TCGTGTAAAA
601	AATGGGTGAA	CAGGTGATAC	AGTCAGTGAA	TATCATATTA	ATTACCGTAA	ACCCAGATGT
661	AGCAAGGCTT	TCAGGGAATT	GTGCAGAGGG	TGCATAACTG	AGAGGGTGAA	AAAGATTTTC
721	AGGGGGGCTT	ATGGCAGGTA	AACAAAATCA	GAAGCAAATA	CCGTGCACAA	TCTGGTTTTT
781	ATTTTTTGGT	ACTACCTCAA	ATTAAAATGA	TGTAATCATC	TGATTTTATT	TAAGAATAGA
841	AGTTAATCAC	AATTTCATTG	ATGGACTTTC	ATTCACACTG	GTATAGATAA	ATAATTCTGT
901	TATATCCTGT	TTCATTACGC	ATTCATCAGG	AGTGCTGTTA	CAGGAGACAA	GAATGTCACA
961	CATCATTTAC	TTGTCGTTAA	AGGGCAAGAA	GCAGGGTTTA	ATTTCAGCGG	GTTGTTCAAC
1021	GCCTGAATCA	ATTGGAAATC	GCTATCAAAA	AGGACGTGAA	GATCAAATAC	AGGTATTGAG
1081	CCTGAATCAT	TCGATGAGCC	GTGACCAGAA	TGTTAATCAT	CAACCCGTCA	GTTTTGTGAA
1141	ACCCATTGAT	AAATCCTCTC	CCCTGTTTGC	TGGATGCCAG	TTTTGTGCAT	TACAGGACAA
1201	GCCAGATGGG	ACAACTGGAG	TTCTTTTATG	AAATCAAGCT	GACCAGTGCC	ACGATTGTGG
1261	ATATTTCCTA	TAATTATCCG	GCATTCAATC	AATGATAATG	GTGCGATACC	CCATGAAGTG
1321	GTGATGCTCG	ATTATAAGTC	CATTTCATGC	AACCACATCG	CCGCAGGACT	TCGGGCTACA
1381	GCATACGCAA	TTAGCCGGAA	GTGAAGAAGC	AAGCCGCTTT	TATCTGGGGT	CTCGAATGTT
1441	AAGCCACTTA	AGAAGCCGCT	GGTTGAAGAA	ACCCCGGTAA	AACCCGCTAA	ACATCATGCC
1501	CGTTATCGTT	GTGTGGATGA	TGACGGCAAT	CTTTTAACCG	AACGCAAGTA	TCGGGTTTGC
1561	CTGCCGGATG	GTCAGATAAA	AGAAGGAAAG	ACTGATAAAC	AAGGTTACAC	CCAATGGCAT
1621	CTTACGGATG	ACAAAAATAA	ACTTGAATTT	CATATTTTAA	AGGATTAATA	CCATGCCAGC
1681	CTATACCGTT	CAGACAAAAA	TAGAATCCAA	CGTACCTGTT	GAAAACCTGC	TTTACGACTT
1741	AACCATTTAT	CGTAAGGATG	CAAAAGGAAA	TTTCCATATC	TTGCTTGATG	TTTTTCAGGA
1801	GAAACTACAG	AGTAATTATG	AAACACAACA	GCATATCACG	CAGGAAATAG	ACGACGATCT
1861	TTCTGTGATT	TATATTATGC	AAATTATGCT	TCACCGCAAA	CATGGCTCAA	ATATATTTCC
1921	GGCACTGCAA	ACCCATTTTA	AGAAAATGTA	TACCCTCGGT	GAATTAACTT	CCGGTAAAGC
1981	CTGTTCGGAG	AAAAAACGGG	AAAATGCCTG	TTATTTTGAA	AGTACAGTTG	AAACAAAACC
2041	TGTCAGCGAC	GGGGATAATA	CCGTTGACTT	AAATATCACT	ATTCCTGAAC	GACCTTTTAT
2101	TGCCAAAGAA	TATCCCATTG	GTCACCCACA	CGATCCATTT	GAAAAAAGTA	AAATTGAATC
2161	ATAAATACAG	GACAGGTTAT	CGAAAAGAAT	TTATCCGGAT	CAAAATGGAG	CAAGTTTATG
2221	TCAGGGCGCG	AGCACACTAT	TTTAGCTGCG	TTTTTAAGAT	GATTATCTCT	TAATGTTCAG
2281	TTTTAATAGT	GTTTTTATCG	AGTGAAATTT	AATCGCACAG	GCAATTCTTT	AGACTTTTAT
2341	AGAAAACTAA	AGAATTAAAG	AACAAGATTG	ACATTTTAAG	TTCAAATATT	AATCAAAGTA
2401	TGCTCGCGCC	CTGAGTTTAT	GTGGCCCTGC	CGCTTTTTTT	TATTGCCTGC	CAATAGATAG
2461	ACCAGATATT	TATGAGCAAG	CGGCACGAGA	ATTATGGCAA	TATGGCCGAA	CTAAAATTGG
2521	TCAACTGGAA	ATTAAGCCGG	GTGAGGGTTG	CCGACATCCT	AAAGGTACTT	TTTATAATCA
2581	ATATGGTGAA	AGAATATCTG	GGTTAGATTG	GCTGACATTG	GCAAGCCTAA	GAGATTCAGA
2641	AAATATGATG	ATGAGGTTGA	TGATGAAGTA	GCTGGTATTA	CAATGTGGGG	AAAATTGACA
2701	GAATGGTTTG	AAAAATCAGG	GTATGAAAAA	GTATTTAGTA	ATGTCGGCTT	ATCCCATTCT
2761	AATATAAATG	ACATAGTAAC	TCTTAGTGAT	TACTATAACA	AAGGATATCA	TGTTGTTACT
2821	TTGATTTCAG	CAGGAATGTT	ATCAGATTTT	GGTGACATAG	AAACATCAGG	AAAAAATCAT
2881	TGGATAGTTT	GGGAAGGAGT	AGTAGAAAAC	TATGAGAAAG	AAAATATCAC	AAATAATTCA
2941	GATCTGAATC	AATATGTAAA	TTTAAATCTG	TTTTCATGGG	GTAAAGTGGA	ACATCAAATT
3001	AAAAAAAACA	AATCACTAGA	TTATGTACTC	AACCATATTT	TTTGAGGGTT	GGTTTTTAAA
3061	CCAATGAAAT	AACATGAAAA	AAATATTAAT	TATTTTTATT	TTTTTACTTT	ATGGTTGTGG
3121	TAATCCAACG	CCAAAAGTTT	TACCAAAATC	AGAGTTTCTT	CCTGATGCAG	TGATAAATGA
3181	ACCATATCAG	GCATCAATTA	CCATCACAGG	AGGTGCATTG	AATGAAAAAA	GCGTTTGGGT
3241	AAAAATTCAT	CCTACTGGCT	CAGGACTAAC	ATGGAATCCA	AAAGATAGTT	CTTTCCTATA
3301	GGGTGGAAAA	AAAGAAATAA	GAAAAGATTA	TCATCATATA	AATATAACAG	GTACCCCAAA
3361	GAAGACAGAA	TTGATAAAAA	TTGAAGTGGT	AGGATTTACA	TTGGGTACAA	TGTACGCACG
3421	GAAAGAGTTC	ACTATAAATT	ATACTATAAA	AGTAAGGGAA	TAATTGTCAC	TATCAGAATG
3481	GTGATTTAAT	TCGCCATTTT	TATACTTTTG	TATACTCTCT	CAACATAATC	AGGATTCTTT

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Fig.2.

3541	CTTATTATTT	TTCATGGTGC	TAAAAACGTT	TATTGCAAAA	ATAAATTAAG	TTAATCAGAT
3601	AAATTATCTG	CATTACTGTT	ATAATCGATA	ACACGATAAC	CTGACTTTCT	GCCTGTTCTT
3661	ATGAACTCGA	AGATAATCCT	TTCTGAGCCT	GAACGAATCA	CATTGCAACC	ACTCGCTTTG
3721	AATCACCCAC	ACCGGGACAT	TCGTACGCGA	GGAACGGGTT	TACTCATGCT	TGCCAGAGGG
3781	AGCAAGCCGT	CCCAGATCAC	CGCTGAAATC	GGATGCAGTC	TCCGGGTTAT	CTGTAATTGG
3841	GTTCACATGT	GGCACAGATA	GCGGGATTAT	TCGGCGGTCA	TGCCGGAGGC	CGGTATCTCG
3901	CCATGACGCC	TGACATGATT	GCCACTGCGC	TCGAAGCCGC	CAGCGCAGAG	TCCCTGACGT
3961	GCGTCGAAGC	CAGGCAGGGT	TTCCCTGCCT	TGTACGCTTG	AAACGCTGGC	GAATACCCTG
4021	AAAAAACAGG	GGCTCCCCTA	TAAACGCCCC	CGCCTGTCGC	TTAAAAAAAG	CGCAATAAAA
4081	CGGAGTTTGC	TGAAAAATCC	GCCTTGCTGA	ATAAAATTAA	GGCCGGAGCA	CAGTCAGGAC
4141	ATTACCGTCT	GGTCTATTTT	GAGTTCTGGG	GGCGTTAAAT	TACACGGATA	ACACGCTGTT
4201	TTACCAGACA	ACGTCAGGCA	GTATCACGCG	AGATGACGTG	ATTGATTTTT	TAGAGCCGGT
4261	GGCCAGACAA	GGGACAACCG	CCTGACATTT	TTAGTGTTGG	ATAATGCGCG	TATCCATCAC
4321	GGGATAGAGG	AAAAAATCAG	AAATGGCGGG	TGACGAGAAC	ACAACCTGTT	TTTATTCTAT
4381	CTTCCCGCTT	ACAGCCCAGA	GCTGTATCTG	ATTGAAATCG	TCTGGAAACA	GGCCAAATAC
4441	GACTGGCGAC	GTTTTATCAC	CTGGACTCAG	GATACAATGG	AATATGAGGT	AAATACTTTA
4501	TTGAAAGGTT	ATGGCGACCA	ATTTGCAATT	AACTTTTCTT	GAGTACTTAG	TAAGAATAGA
4561	GTCAGTCGAG	GTTTTTTCAT	TTCGGGTCGT	GGGGATGATA	CTGAAAATTT	GTTTGTAATC
4621	TCTGAAAATT	GCTGTTTCTG	TGGCTACGTC	TGTCTTTTGG	GATATTGTTT	CCATCAAGTC
4681	TGTCAACATA	CTGTTAAGTT	AGATGTTGAT	AAAAGAGACT	GAATTATAAT	ACAAAACAAT
4741	AAATCACTTG	GACAATATTT	TATTTCACAT	GAGACATTAA	GGTTGATTTT	CCCAATCTGG
4801	TCAGTTATAA	CCGAATAAGG	ATCTTGAAAA	ATCATGGGAT	CTTACTTTTA	TCAAATGAAG
4861	TTAACGTAAA	AGTTGATAAA	GAAAATTATT	TAATTCTAAG	TGCCGTTGGC	ATAAATATTT
4921	TGTGTTTTGT	TAATGAATGA	ATAACCAGGT	AAGCTGGATT	TTCATTTTTT	AATTACTCGT
4981	TACAATATGC	TATTTATTTA	TATAAAGAGT	TTGTGCCCAT	TTAACCAGTA	AACAAATTTG
5041	TTCAACCGTA	ACTTAGCTTC	ATCGACTTTT	GGCCTCGCCT	GGTCAGAATC	TAGGGCCGTT
5101	ATCCTATTTA	TTTATGATAA	ATAAAATTTA	ATTATCTTTA	ATAAGCTGAA	TATGTGGATT
5161	TGTGCTCAAT	CTTGGATTCA	AGTATGTATT	CCTTTTGGTA	CCCTGCTTTA	TTTTAAGGCA
5221	GATGAAGAGG	ATGCCAACAT	GACACAATAT	CGATTACGAC	TGTAACATTA	AAGTCAGTTA
5281	TAAATTTTAT	GATTAAAATG	AAATTTTAGT	AGAAAATCGT	ATTCTATTCC	GCCATTTACA
5341	ATAGCATCCT	CTTTAATATC	ATTAATCTCA	GATAAAACAA	ATAATTACAA	TGTGAATAGA
5401	ATAATGACTT	ACAAAATAAG	CACTAAATCT	TCAGATGAAC	TCTTAACTGA	CAACACTATT
5461	TTATAAAATA	ATTGAGGTTA	TTATGTATAG	CACGGCTGTA	TTACTCAATA	AAATCAGTCC
5521	CACTCGCGAC	GGTCAGACGA	TGACTCTTGC	GGATCTGCAA	TATTTATCCT	TCAGTGAACT
5581	GAGAAAAATC	TTTGATGACC	AGCTCAGTTG	GGGAGAGGCT	CGCCATCTCT	ATCATGAAAC
5641	TATAGAGCAG	AAAAAAAATA	ATCGCTTGCT	GGAAGCGCGT	ATTTTTACCC	GTGCCAACCC
5701	ACAATTATCC	GGTGCTATCC	GACTCGGTAT	TGAACGAGAC	AGCGTTTCAC	GCAGTTATGA
5761	TGAAATGTTT	GGTGCCCGTT	CTTCTTCCTT	TGTGAAACCG	GGTTCAGTGG	CTTCCATGTT
5821	TTCACCGGCT	GGCTATCTCA	CCGAATTGTA	TCGTGAAGCG	AAGGACTTAC	ATTTTTCAAG
5881	CTCTGCTTAT	CATCTTGATA	ATCGCCGTCC	GGATCTGGCT	GATCTGACTC	TGAGCCAGAG
5941	TAATATGGAT	ACAGAAATTT	CCACCCTGAC	ACTGTCTAAC	GAACTGTTGC	TGGAGCTATT
6001	ACCCGCAAGA	CCGGAGGTGA	TTCGGACGCA	TTGATGGAGA	GCCTGTCAAC	TTACCGTCAG
6061	GCCATTGATA	CCCCTTACCA	TCAGCCTTAC	GAGACTATCC	GTCAGGTCAT	TATGACCCAT
6121	GACAGTACAC	TGTCAGCGCT	GTCCCGTAAT	CCTGAGGTGA	TGGGGCAGGC	GGAAGGGGCT
6181	TCATTACTGG	CGATTCTGGC	CAATATTTCT	CCAGAACTGT	ATAACATTTT	GACCGAAGAG
6241	ATTACGGAAA	AGAACGCTGA	TGCTTTATTT	GCGCAAAACT	TCAGTGAAAA	TATCACGCCC
6301	GAAAATTTCG	CGTCACAATC	ATGGATAGCC	AAGTATTATG	GTCTTGAACT	TTCTGAGGTG
6361	CAAAAATACC	TCGGGATGTT	GCAGAATGGC	TATTCTGACA	GCACCTCTGC	TTATGTGGAT
6421	AATATCTCAA	CGGGTTTAGT	GGTCAATAAT	GAAAGTAAAC	TCGAAGCTTA	CAAAATAACA
6481	CGTGTAAAAA	CAGATGATTA	TGATAAACAT	GTAAATTACT	TTGATCTGAT	GTATGAAGGA
6541	AATAATCAAT	TCTTTATATG	TGCTAATTTT	AAGATATCGA	GAGAATTTGG	GGCGACTCTT
6601	AGGAAAAACT	CAGGGACAAG	TGGCATTGTC	GGCAGCCTTT	CCGGTCCCCT	GGTAGCCAAT
6661	ACTAATTTCA	AAAGCAATTA	CTTAAGTAAC	ATATCTGATA	ATGAATACAG	AAATGGCGTA
6721	AAAATATATG	CCTATCGCTA	TACGTCTTCC	ACCAGCGCCA	CAAATCAGGG	CGGCGGAATA
6781	TTCACTTTTG	AGTCTTATCC	CCTGACTATA	TTTGCGCTCA	AACTGAATAA	AGCCATTCGC
6841	TTGTGCCTGA	CTAGCGGGCT	TTCACCGAAT	GAACTGCAAA	CTATCGTACG	CAGTGACAAT
6901	GCACAAGGCA	TCATCAACGA	CTCCGTTCTG	ACCAAAGTTT	TCTATACTCT	GTTCTACAGT
6961	CACCGTTATG	CACTGAGCTT	TGATGATGCA	CAGGTACTGA	ACGGATCGGT	CATTAATCAA
7021	TATGCCCGAC	GATGACAGTG	TCAGTCATTT	TAACCGTCTC	TTTAATACCC	CGCCGCTGAA
7081	AGGGAAAATC	TTTGAAGCCG	ACGGCAACAC	GGTCAGCATT	GATCCGGATG	AAGAACAATC
7141	TACCTTTGCC	CGTTCAGCCC	TGATGCGTGG	TCTGGGGATC	AACAGTGGTG	AACTGTATCA
7201	GTTAGGCAAA	CTGGCGGGTG	TATTGGACAC	ACAAAATATC	CTCACACTTT	CTGTCCCTGT
7261	TATATCTTCA	CTGTATCGCC	TCACGTTACT	GGCCCGTGCC	CATCAGCTGA	CGGTTAATGA
7321	ACTGTGTATG	CTTTATGGTT	TTTCGCCGTT	CAATGGCAAA	ACAACGGCTT	CTTTGTCTTC

SUBSTITUTE SHEET (RULE 26)

BNSDOCID: <WO___9808388A1_I_>

Fig.2.

7381 CGGGGAGTTG TCACGGCTGG TTATCTGGTT GTATCAGGTG ACGCAGTGGC TGACTGAGGG
7441 CGGAAATCAC CACTGAAGCG ATCTGGTTAT TATGTACGCC AGAGTTCAGC GGGAATATTT
7501 CACCGGAAAT CAGTAATCTG CTTAATACTC TCCGACCCCG TATTAGTGAA GACATGGCAC
7561 AAAGTAGTGA CCGGGAGCTT CAGGCTGAAA TTCTCGCGCC GTTTATTGCT GCAACGCTGC
7621 ATCTGGCGTC ACCAGATATG GCGCGGTATA TCCTGTTGTG GACTGATAAC CTGCGGCCGG
7681 GCGGCCTGAA TATCGCCGGA TTTATGATGC TGGTGCTGAA AGAGACGCTG AGTGATGAGG
7741 AAACGACCCA ACTGGTTCAA TTCTGCCATG TAATGGCACA GTTATCGCTT TCCGTGCAGA
7801 CACTGCGTCT CAGTGAAGCA GAGCTTTCTG TGCTGGTCAT TTCCGATTTT GTGGTACTGG
7861 GTGCGAGAAG CCAACCGCCG GACAACACAA TATTGATACT CTGTTCTCAC TCTACCGATT
7921 CCACCAGTGG ATTAATGGGC TGGGAAATCC CGGCTCTGAC ACGCTGGATA TGCTGCGCCA
7981 AGCAGACACT CACGGGCGAC AGACTGGGCC TCCGTGATGG GGCTGGACAT CAGTATGGTA
8041 ACGCAGGCCA TGGGTTCCCG CCGGCGTGAA CCAACTTCAG TGTTGGCAGG ATATCAACCC
8101 CGTGTTGCAG TGGATACATG TGGCATCAGC ACTGCTCACT GATGCCGTCG GTTATCCGTA
8161 CGCTGGTGAA TATCCGTTAC GTGACTGCAT TAAACAAAGC CGAGTCGAAT CTGCCTGCCT
8221 GGGATAAGTG GCAGACGCTG GCAGAAAATA TGGCAGCCGG ACTGAGTACA CAACAGGCTC
8281 AGACGCTGGC GGATTATACC GCAGAGCGCC TGAGTAACGT GTTGTGCAAT TGGTTTCTGG
8341 CGAATATCCA GCCAGAAGGG GTGTCCCTGC ACAGCCGGGA TGACCTGTAC AGCTATTTCC
8401 TGATTGATAA TCAGGTCTCT TCTGCCATAA AAACCACCCG ACTGGCAGAG GCCATTGCCG
8461 GTATTCAGCT CTACATCAAC CGGGCGCTGA ACCGGATAGA GCCTAATGCC CGTGCCGATG
8521 TGTCAACCCG CCAGTTTTTT ACCGACTGGA CGGTGAATAA CCGTTACAGC ACCTGGGGCG
8581 GGGTGTCGCG GCTGGTTTAT TATCCGGAAA ATTACATTGA CCCGACCCAG CGTATCGGGC
8641 AGACCCGGAT GATGGATGAA CTGCTGGAAG ATATCAGCCA GAGTCAGCTC AGCCGGGACA
8701 CGGTGGAAGA GGCCTTTAAA ACTTACCTGA CCGCTTTGAA ACCGTGGCAG ACCTGAAAGT
8761 TGTCAGCGCT ATCACCGACA ACGTCAACAG CAACACCGGA CTGACCTGGT TTGTCGGCCA
8821 AACGCGGGAG AACCTGCCGG AATATTACTG GCGTAACGTG CATATATCAC GGATGCAGGC
8881 GGGTGAACTG GCCGCCGATG CCTGGAAAGA TTGGACGAAG ATTGATACAG CGGTCAACCC
8941 ATACAAGGAT GCAATACGTC CGGTCATATT CAGGGAACGT TTGCACCTTA TCGTGGGTAG
9001 AAAAAGAGGA AGTGGCGAAA AATGGTACTG ATCCGGTGGA AACCTATGAC CGTTTTACTC
9061 TGAAACTGGC GTTTCTGCGT CATGATGGCA GTTGGAGTGC CCCCTGGTCT TACGATATCA
9121 CAACGCAGGT GGAGGCGGTC ACTGACAAAA AACCTGACAC TGAACGGCTG GCGCTGGCCG
9181 CATCAGGCTT TCAGGGCGAG GATACTCTGC TGGTGTTTGT GTACAAAACC GGGGTGAGTT
9241 ACCCGGATTT TGGCGACAAC AATAAAAATG TGGCAGGCAT GACCATTTAC GGCGATGGCT
9301 CCTTCAAAAA GATGGAGAAC ACAGCACTCA GCGTTACAGC CAACTGAAAA ATACCTTTGA
9361 TATCATTCAT ACTCAAGGCA ACGACTTGGT AAGAAAGGCC AGCTATCGTT TCGCGCAGGA
9421 TTTTGAAGTG CCTGCCTCGT TGAATATGGG TTCTGCCATC GGTGATGATA GTCTGACGGT
9481 GATGGAAAAC GGGAATATTC CGCAGATAAC CAGTAAATAC TCCAGCGATA ACCTTGCTAT
9541 TACGCTACAT AACGCCGCTT TCACTGTCAG ATATGATGGC AGTGGCAATG TCATCAGAAA
9601 CAAACAAATC AGCGCCATGA AACTGACGGG GTTGGATGAA AGTCCCAGTA CGGCAATGCA
9661 TTTATCATCG CAAATACCGT TAAACATTAT GGCGGTTACT CTGATCTGGG GGGCCCGATC
9721 ACCGTTTTTA TTAAAACGGA AAAACTATAT TGCATCAGTT CAAGGCCACT TGATGAACGC
9781 AGATTACACT AGGCGTTTGA TTCTAACACC AGTTGAAAAT AATTATTATG CCAGATTGTT
9841 CGAGTTTCCA TTTTCTCCAA ACACAATTTT AAACACCGTT TTCACGGTTG GTAGCAATAA
9901 AACCAGTGAT TTTAAAAAGT GCAGTTATGC TGTTGATGGT AATAATTCTC AGGGCTTCCA
9961 GATATTTAGT TCCTATCAAT CATCCGGCTG GCTGGATATT GACACAGGTA TTAACAATAC
10021 TGATGTCAAA ATTACGGTGG TAGCTGGCAG TAAAACCCAC ACCTTTACGG CCAGTGACCA
10081 TATTGCTTCC TTGCCGGCAA ACAGTTTTGA TGCTATGCCG TACACCTTTA AGCCACTGGA
10141 AATCGATGCT TCATCGTTGG CCTTTACCAA TAATATTGCT CCTCTGGATA TCGTTTTTGA
10201 GACCAAAGCC AAAGACGGGC GAGTGCTGGG TAAGATCAAG CAAACATTAT CGGTGAAACG
10261 GGTAAATTAT AATCCGGAAG ATATTCTGTT TCTGCGTGAA ACTCATTCGG GTGCCCAATA
10321 TATGCAGCTC GGGGTGTATC GTATTCGTCT TAATACCCTG CTGGCTTCTC AACTGGTATC
10381 CAGAGCAAAC ACGGGCATTG ATACTATCCT GACAATGGAA ACCCAGCGGT TACCGGAACC
10441 TCCGTTGGGA GAAGGCTTCT TTGCCAACTT TGTTCTGCCT AAATATGACC CTGCTGAACA
10501 TGGCGATGAG CGGTGGTTTA AAATCCATAT CGGGAATGTT GGCGGTAACA CGGGAAGGCA
10561 GCCTTATTAC AGCGGAATGT TATCCGATAC GTCGGAAACC AGTATGACAC TGTTTGTCCC
10621 TTATGCCGAA GGGTATTACA TGCATGAAGG TGTCAGATTG GGGGTTGGAT ACCAGAAAAT
10681 TACCTATGAC AACACTTGGG AATCTGCTTT CTTTTATTTT GATGAGACAA AACAGCAATT
10741 TGTATTAATT AACGATGCTG ATCATGATTC AGGAATGACG CAACAGGGGA TCGTGAAAAA
10801 TATCAAGAAA TACAAAGGAT TTTTGAATGT TTCTATCGCA ACGGGCTATT CCGCCCCGAT
10861 GGATTTCAAT AGTGCCAGCG CCCTCTATTA CTGGGAATGT TCTATTACAC CCCGATGATG
10921 TGCTTCCAGC GTTTGCTACA GGAAAAACAA TTCGACGAAG CCACACAATG GATAAACTAC
10981 GTCTATAATC CCGCCGGCTA TATCGTTAAC GGAGAAATCG CCCCCTGGAT CTGGAACTGC
11041 CGGCCGCTGG AAGAGACACT CCTGGAATGC CAATCCGTTG GATGCCATTG ATCCGGATGC
11101 CGTCGCACAA TATGACCCGA CACACTATAA AGTTGCCACC TTTATGCGCC TGTTGGATCA
11161 ACTTATTCTG CGCGGCGATA TGGCCTATCG CGAACTGACC CGCGATGCGT TGAATGAAGC

SDOCID: <WO__ 9808388A1_I_>

Fig.2.

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11221  CAAGATGTGG TATGTGCGTG CTTTGGAATT GCTGGGTGAT GAGCCGGAGG ATTACGGCAG
11281  CCAACAGTGG GCCGCACCGT CTCTTTCCGT GGCGGGCAAC CACACTGTGC AAGCGGGCTA
11341  TCAACAAGAC CTTACGGCGC TAGACAACGG AGAAGGTTGC ACTCAACCCC GCAACGCTAA
11401  CTCGTTGGTG GTTTGGTCCT GCCGGAATAT AACCCGGAAT CAACCGATTA CTGGCAAACC
11461  TGCGTTTGCG CCTGGTTAAC CTGCGCCATA ATCCTTCCAT GACGGGCAAC CGTTATCGCT
11521  GGCGAATTAC GCGAGCCTAC GATCCGAAAG CGCTGCTCAC CAGTATGGTA CAGCCTTCTC
11581  AGGGCGGTAG TGCAGTGCTG CCCGGCACAT TGTCGTTATA CCGCTTCCCG GTGATGCTGG
11641  AGCGGGCCCG CAATCTGGTA GCGCAATTAA CCCAGTTCGG CACCTCTCTG CTCAGTATGG
11701  CAGAGCATGA TGATGCCGAT GAACTCACCA CGTTGCTACT ACAGCAGGGT ATGGAACTGG
11761  CGACACAGAG CATCCGTATT CAGCAACGAA CTGTCGATGA AGTGGATGCT GATATTGCTG
11821  TATTGGCAGA GAGCCGCCGC AGTGCACAAA ATCGTCTGGA AAAATACCAG CAGCTGTATG
11881  ACGAGGATAT CAACCACGGA GAACAGCGTG CGATGTCACT GTTTGATGCG GCGGCAGGTC
11941  AGTCTCTGGC CGGGCAGGCG CTCTCAGTAG CAGAAGGGGT GGCTGACTTA GTTCCAAACG
12001  TGTTCGGTTT CGCTTGTGGC GGCAGTCGTT GGGGGGCAGC ACTGCGTGCT TCCGCCTCCG
12061  TGATGTCGCT TTCTGCCACA GCTTCCCAAT ATTCCGCAGA CAAAATCAGC CGTTCGGAAG
12121  CCTACCGCCG CCGCCGTCAG GAGTGGGAAA TTCAGCGTGA TAATGCTGAC GGTGAAGTCA
12181  AACAAATGGA TGCCCAGCTG GAAAGCCTGA AAATACGCGG CGAAGCAGCA CAGATGCAGG
12241  TGGAATATCA GGAGACCCAG CAGGCCCATA CTCAGGCTCA GTTAGAGCTG TTACAGCGTA
12301  AATTCACAAA CAAAGCGCTT TACAGTTGGA TGCGCGGCAA GCTGAGTGCT ATCTATTACC
12361  AGTTCTTTGA CCTGACCCAG TCCTTCTGCC TGATGGCACA GGAAGCGCTG CGCCGCGAGC
12421  TGACCGACAA CGGTGTTACC TTTATCCGGG GTGGGGCCTG GAACGGTACG ACTGCGGGTT
12481  TGATGGCGGG TGAAACGTTG CTGCTGAATC TGGCAGAAAT GGAAAAAGTC TGGCTGGAGC
12541  GTGATGAGCG GGCACTGGAA GTGACCCGTA CCGTCTCGTT GGCACAGTTC TATCAGGCCT
12601  TATCATCAGA CAACTTTAAT CTGACCGAAA AACTCACGCA ATTCCTGCGT GAAGGGAAAG
12661  GCAACGTAGG AGCTTCCGGC AATGAATTAA AACTCAGTAA CCGCCAGATA GAAGCCTCAG
12721  TGCGATTGTC TGATTTGAAA ATTTTCAGCG ATACCCCGGA AAGCTTTGGC AATACCCGTC
12781  AGTTGAAACA AGTGAGTGTC ACCTTGCCGG CGCTGGTTGG TCCGTATGAA GATATCCGGG
12841  CGGTGCTGAA TTACGGCGGC AGCATCGTCA TGCCACGCGG TTGCAGTGCT ATTGCTCTCT
12901  CCCACGGCGT GAATGACAGT GGTCAATTTA TGCTGGATTT CAACGATTCC CGTTATCTGC
12961  CGTTTGAAGG TATTTCCGTG AATGACAGCG GTAGCCTGAC GTTGAGTTTC CCGGATGCGA
13021  CTGATCGACA GAAAGCGCTG CTGGAGAGCC TGAGCGATAT CATTCTGCAT ATCCGCTATA
13081  CCATTCGTTC TTAATTAAAA CATTGTGATA GGCAGGCTCC TGAGGGAGCC TGTTTAAGGA
13141  GTTTTTATGC AGGGTTCAAC ACCTTTGAAA CTTGAAATAC CGTCATTGCC CTCTGGGGGC
13201  GGATCACTAA AAGGAATGGG AGAAGCACTC AATGCCGTCG GAGCGGAAGG GGAGCGTCAT
13261  TTTCACTGCC CTTGCCGATC TCTGTCCGGC GTGGTCTGGT GCCGGTGCTA TCACTGAATT
13321  ACAGCAGTAC TGCTGGCAAT GGGTCATTCG GGATGGGGTG GCAATGTGGG GTTGGTTTTA
13381  TCAGCCTGCG TACCGCCAAG GGCGTTCCGC ACTATACGGG ACAAGATGAG TATCTCGGGC
13441  CGGATGGGGA AGTGTTGAGT ATTGTGCCGG ACAGCCAAGG GCAACCAGAG CAACGCACCG
13501  CAACCTCACT GTTGGGGACG GTTCTGACAC AGCCGCCTAC TGTTACCCGC TATCAGTCCC
13561  GCGTGGCAGA AAAAATCGTT CGTTTAGAAC ACTGGCAGCC ACAGCAGAGA CGTGAGGAAG
13621  AGACGTCTTT TTGGGTACTT TTTACTGCGG ATGGTTTAGT GCACCTATTC GGTAAGCATC
13681  ATCATGCACG TATTGCTGAC CCGCAGGATG AAACCAGAAT TGCCCGCTGG CTGATGGAGG
13741  AAACCGTCAC GCATACCGGG GAACATATTT ACTATCACTA TCGGGCAGAA GACGATCTTG
13801  ACTGTGATGA GCATGAACTT GCTCAGCATT CAGGTGTTAC GGCCCACCGT TATCCTGGCA
13861  AGTCCACTAT GGCAATACTC AGCCGGAAAC CGCTTTTTTC GCGGTAAAAT CAGGTATCCC
13921  TGTTGATAAT GACTGGTTGT TTCATCTGGT ATTTGATTAC GGTGAGCGCT TATCTTCGCT
13981  GAACTCCGTA CCCGAATTCA ATGTGTCAGA AAACAATGTG TCTGAAAACA ATGTGTCTGA
14041  AAAATGGCGT TGTCGTCCGG ACAGTTTCTC CCGCTATGAA TATGGGTTTG AAATTCGAAC
14101  CCGTCGCTTG TGTCGCCAAG TTCTGATGTT TCATCAGCTG AAAGCGCTGG CAGGGGAAAA
14161  GGTTGCAGAA GAAACACCGG CGCTGGTTTC CCGTCTTATT CTGGATTATG ACCTGAACAA
14221  CAAGGTTTCC TTGCTGCAAA CGGCCCGCAG ACTGGCCCAT GAAACGGACG GTACGCCAGT
14281  GATGATGTCC CCGCTGGAAA TGGATTATCA ACGTGTTAAT CATGGCGTGA ATCTGAACTG
14341  GCAGTCCATG CCGCAGTTAG AAAAAATGAA CACGTTGCAG CCATACCAAT TGGTTGATTT
14401  ATATGGAGAA GGAATTTCCG GCGTTACTTT ATCAGGATAC TCAGAAAGCC TGGTGGTACC
14461  GTGCTCCGGT ACGGGATATC ACTGCCGAAG GAACGAATGC GGTTACCTAT GAGGAGGCGA
14521  AACCACTGCC ACATATTCCG GCACAACAGG AAAGCGCGAT GTTGTTGGAC ATCAATGGTG
14581  ACGGGCGTCT GGATTGGGTG ATTACGGCAT CAGGGTTACG GGGCTACCAC ACCATGTCAC
14641  CGGAAGGTGA ATGGACACCC TTTATTCCAT TATCCGCTGT GCCAATGGAA TATTTCCATC
14701  CGCAGGCAAA ACTGGCTGAT ATTGATGGGG CTGGGCTGCC TGACTTAGCG CTTATCGGGC
14761  CAAATAGTGT ACGTGTCTGG TCAAATAATC CGGCAGGATG GGATCGCGCT CAGGATGTTA
14821  TTCATTTGTC AAATAAGCCA CTGCCGGTTC CCGGCAAAAA TAAGCGTCAT CTTGTCGCAT
14881  TCAGTGATAT GACAGGCTCC GGGCAATCAC ATCTGGTGGA AGTTACGGCA AATAGCGTGC
14941  GCTACTGGCC GAACCTGGGG CATGGAAAAT TTGGTGAGCC TCTGATGATA ACAGGCTTCC
15001  AAATTACGGG GAAACGTTTA ACCCCCACAG ACTGTATATG GTAGACCTAA ATGGCTCAGG
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SUBSTITUTE SHEET (RULE 26)

Fig.2.

15061 CACCACCCGA TTTTATTTAT GCCCGCAATA CTTACCTTGA ACTCTATGCC AATGAAAGCG
15121 GCAATCATTC TGCTGAACCT CAGCGTATTG ATCTGCCGGA TGGGGTACGT TTTGATGATA
15181 CTTGTCGGTT ACAAATAGCG GATACACAAG GATTAGGGAC TGCCAGCATT ATTTTGACGA
15241 TCCCCCATAT GAAGGTGCAG CACTGGCGAT TGGATATGAC CATATTCAAG CCTTGGCTGC
15301 TGAATGCCGT CAATAACAAT ATGGGAACAG AAACCACGCT GTATTATCGC AGCTCTGCCC
15361 AGTTCTGGCT GGATGAGAAA TTACAGGCTT CTGAATCCGG GATGACGGTG GTCAGCTACT
15421 TACCGTTCCC GGTGCATGTG TTGTGGCGCA CGGAAGTGCT GGATGAAATT TCCGGTAACC
15481 GATTGACCAG CCATTATCAT TACTCACATG GTGCCTGGGA TGGTCTGGAA CGGGAGTTTC
15541 GTGGTTTTGG GCGGGTGACG CAAACTGATA TTGATTCACG GGCGAGTGCG ACACAGGGGA
15601 CACATGCTGA ACCACCGGCA CCTTCGCGCA CGGTTAATTG GTACGGCACT GGCGTACGGG
15661 AAGTCGATAT TCTTCTGCCC ACGGAATATT GGCAGGGGGA TCAACAGGCA TTTCCCCATT
15721 TTACCCCACG CTTTACCCGT TATGACGAAA AATCCGGTGG TGATATGACG GTCACGCCGA
15781 GCGAACAGGA AGAATACTGG TTACATCGAG CCTTAAAAGG ACAACGTTTA CGCAGTGAGC
15841 TGTATGGGGA TGATGATTCT ATACTGGCCG GTACGCCTTA TTCAGTGGAT GAATCCCGCA
15901 CCCAAGTACG TTTGTTACCG GTGATGGTAT CGGACGTGCC TGCGGTACTG GTTTCGGTGG
15961 CCGAATCCCG CCAATACCGA TATGAAGGGG TTGTTACCGA TTCCACAGTG CAGCCAAAAG
16021 ATTGTCCTTA AATATGATGC GTTAGGATTT CCGCAGGACA ATCTTGAGAT TGCCTATTCG
16081 AGACGTCCAC AGCCTGAGTT CTCGCCTTAT CCGGATACCC TGCCCGAAAC ACTTTTCACC
16141 AGCAGTTTCG ACGAACAGCA GATGTTCCTT CGTCTGACAC GCCAGCGTTT TTCTTATCAC
16201 CATCTGAATC ATGATGATAA TACGTGGATC ACAGGGCTTA TGGATACCTC ACGCAGTGAC
16261 GCACGTATTT ATCAAGCCGA TAAAGTGCCG GACGGTGGAT TTTCCCTTGA ATGGTTTTCT
16321 GCCACAGGTG CAGGAGCATT GTTGTTGCCT GATGCCGCAG CCGATTATCT GGGACATCAG
16381 CGTGTAGCAT ATACCGGTCC AGAAGAGCAA CCCGCTATTC CTCCGCTGGT GGCATACATT
16441 GAAACCGCAG AGTTTGATGA ACGATCGTTG GCGGCTTTTG AGGAGGTGAT GGATGAGCAG
16501 GAGCTGACAA AACAGCTGAA TGATGCGGGC TGGAATACGG CAAAAGTGCC GTTCAGTGAA
16561 AAGACAGATT TCCATGTCTG GGTGGGACAA AAGGAATTTA CAGAATATGC CGGTGCAGAC
16621 GGATTCTATC GGCCATTGGT GCAACGGGAA ACCAAGCTTA CAGGTCAAAC GACAGTGACG
16681 TGGGATAGCC ATTACTGTGT TATCACCGCA ACAGAGGATG CGGCTGGCCT GCGTATGCAA
16741 GCGCATTACG ATTATCGATT TATGGTTGCG GATAACACCA CAGATATCAA TGATAACTAT
16801 CACACCGTGA CGTTTGATGC ACTGGGGACG GTAACCAGCT TCCGTTTCTG GGGGACTGAA
16861 AACGGTGAAA AACAAGGATA TACCCCTGCG GAAAATGAAA CTGTCCCCTT TATTGTCCCC
16921 ACAACGGTGG ATGATGCTCT GGCATTGAAA CCCGGCATAC CTGTTGCAGG GCTGATGGTT
16981 TATGCCCCTC TGAGCTGGAT GGTTCAGGCC AGCTTTTCTA ATGATGGGGA GCTTTATGGA
17041 GAGCTGAAAC CGGCTGGGAT CATCACTGAA GATGGTTATC TCCTGTCGCT TGCTTTTCGC
17101 CGCTGGCATC AAAATAACCC TGCCGCTGCC ATGCCAAAGC AAGTCAATTC ACAGAACCCA
17161 CCCCATGTAC TGAGTGTGAT CACCGACCGC TATGATGCCG ATCCGGAACA ACAATTACGT
17221 CAAACGTTTA CGTTTAGTGA TGGTTTTGGG CGAAACCTTA CAAACAGCCG TACGCCATGA
17281 AAGTGGTGAA GCCTGGGTAC CTGATGAGTA TGGAGCCAAT GTGGCTGAAA ATCAAGGCGC
17341 CCCTGAAACG GGCGATTACA AATTTCCCGT TGGGCAATTT CCCGGACGTA CAGAATATTA
17401 ACGGGAAAAG GCAAAGCCCC TGCGTTACGT TTCAAACCGT ATTCCTGAAA TAATTTGGGC
17461 AACTATGTCA AGTTGACCAA AAAATGCCCG GCAGGATATG TATGCCGATA CCCATTACTA
17521 TGATCCGTTG GGGCGTGAAT ATCAGGTTAT CACGCCAAAG GCGGGTTGCG TCGATCCTTA
17581 TTCACTCCCT GGTTTGTGGT GAATGAAGTT GAAAATGACA CTCCCGGTGA ATGACAGCAT
17641 AAAGCTCAGT GATGCCTGTT CACTGAACAG ACATCACTCC ATTTAGGAAT GAATCATGAA
17701 GAATTTCGTT CACAGCAATA CGCCATCCGT CACCGTACTG GACAACCGTG GTCAGACAGT
17761 ACGCGAAATA GCCTGGTATC GGCACCCCGA TACACCTCAG GTAACCGATG AACGCATCAC
17821 CGGTTATCAA TATGATGCTC AAGGATCTCT GACTCAGAGT ATTGATCCGC GATTTTATGA
17881 ACGCCAGCAG ACAGCGAGTG ACAAGAACGC CATTACACCC AATCTTATTC TCTTGTCATC
17941 ACTCAGTAAG AAGGCATTGC GTACGCAAAG TGTGGATGCC GGAACCCGTG TCGCCCTGCA
18001 TGATGTTGCC GGGCGTCCCG TTTTAGCTGT CAGCGCCAAT GGCGTTAGCC GAACGTTTCA
18061 GTATGAAAGT GATAACCTTC CGGGACGATT GCTAACGATT ACCGAGCAGG TAAAAGGAGA
18121 GAACGCCTGT ATCACGGAGC GATTGATTTG GTCAGGAAAT ACGCCGGCAG AAAAAGGCAA
18181 TAATTTGGCC GGCCAGTGCG TGGTCCATTA TGATCCCACC GGAATGAATC AAACCAACAG
18241 CATATTGTTA ACCAGCATAC CCTTGTCCAT CACACAGCAA TTAGTGAAAG ATGACAGCGA
18301 AGCCGATTGG CACGGTATGG ATGAATTTGG CTGGAAAAAC GCGCTGGCGC CGGAAAGCTT
18361 CACTTCTGTC AGCACAACGG ATGCTACCGG CACGGTATTA ACGAGTACAG ATGCTGCCGG
18421 AAACAAGCAA CGTATCGCCT ATGATGTGGC CGGTCTGCTT CAAGGCAGTT GGTTGGCGCT
18481 GAAGGGGAAA CAAGAACAAG TTATCGTGAA ATCCCTGACC TATTCGGCTG CCAGCCAGAA
18541 GCTACGGGAG GAACATGGTA ACGGGATAGT GACTACATAT ACCTATGAAC CCGAGACGCA
18601 ACGAGTTATT GGCATAAAAA CAGAACGTCC TTCCGGTCAT GCCGCTGGGG AGAAAATTTT
18661 ACAAAACCTG CGTTATGAAT ATGATCCTGT CGGAAATGTG CTGAAATCAA CTAATGATGC
18721 TGAAATTACC CGCTTTTGGC GCAACCAGAA AATTGTACCG GAAAATACTT ACACCTATGA
18781 CAGCCTGTAC CAGCTGGTTT CCGTCACTGG GCGTGAAATG GCGAATATTG GCCGACAAAA
18841 AAACCAGTTA CCCATCCCCG CTCTGATTGA TAACAATACT TATACGAATT ACTCTCGCAC

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Fig.2.

18901	TTACGACTAT	GATCGTGGGG	GAATCTGACC	AGAATCGCAT	AATTCACGAT	CACCGGTAAT
18961	AACTATACAA	CGAACATGAC	CGTTTCAGAT	CACAGCAACC	GGGCTGTACT	GGAAGAGCTG
19021	GCGCAAGATC	CCACTCAGGT	GGATATGTTG	TTCACCCCCG	GCGGGCATCA	GACCCGGCTT
19081	GTTCCCGGTC	AGGATCTTTT	CTGGACACCC	CGTGACGAAT	TGCAACAAGT	GATATTGGTC
19141	AATAGGGAAA	ATACGACGCC	TGATCAGGAA	TTCTACCGTT	ATGATGCAGA	CAGTCAGCGT
19201	GTCATTAAGA	CTCATATTCA	GAAGACAGGT	AACAGTGAGC	AAATACAGCG	AACATTATAT
19261	TTGCCAGAGC	TGGAATGGCG	CACGACATAT	AGCGGCAATA	CATTAAAAGA	GTTTTTGCAG
19321	GTCATCACTG	TCGGTGAAGC	GGGTCAGGCA	CAAGTGCGGG	TGCTGCATTG	GGAAACAGGC
19381	AAACCGGCGG	ATATCAGCAA	TGATCAGCTG	CGCTACAGTT	ATGGCAACCT	GATTGGCAGT
19441	AGCGGGCTGG	AATTGGGACA	GTGACGGGCA	GATCATTAGT	CAGGAAGAAT	ATTACCCCTA
19501	TGGGGGAACC	GCCGTGTGGG	CACCCGAAAT	CAGTCAGAAG	CTGATTACAC	AAGCCGGCGT
19561	TATTCTGGCA	AAGAGCGGGA	TGCAACAGGG	TTGTATTACT	ACGGCTATCG	TTATTATCAA
19621	TCGTGGACAG	GGCGATGGTT	GAGTGTAGAT	CCTGCCGGTG	AGGCCGATGG	TCTCAATTTG
19681	TTCCGAATGT	GCAGGAATAA	CCCCATCGTT	TTTTCTGATT	CTGATGGTCG	TTTCCCCGGT
19741	CAGGGTGTCC	TTGCCTGGAT	AGGGAAAAAA	GCGTATCGAA	AGGCAGTCAA	CATCACGACA
19801	GAACACCTGC	TTGAACAAGG	CGCTTCCTTT	GATACGTTCT	TGAAATTAAA	CCGAGGATTG
19861	CGAACGTTTG	TTTTGGGTGT	GGGGGTACAA	GTCTGGGGGT	GAAGCGGCCA	CGATTGCAGG
19921	AGCGTCGCCT	TGGGGGATCG	TCGGGGCTGC	CATTGGTGGT	TTTGTCTCCG	GGGCGGTGAT
19981	GGGGTTTTTC	GCGAACAACA	TCTCAGAAAA	AATTGGGGAA	GTTTTAAGTT	ATCTGACGCG
20041	TAAACGTTCT	GCTCCTGTTC	AGGTAGGCGC	TTTTGTTGTC	ACATCGCTTG	TGACGTCTGC
20101	ACTATTTAAC	AGCTCTTCGA	CAGGTACCGC	CATTTCCGCA	GCAACAGCGG	TCACCGTTGG
20161	AGGATTAATG	GCTTTAGCCG	GAGAACATAA	CACGGGCATG	GCTATCAGTA	TTGCCACACC
20221	CGCCGGACAA	AGTACGCTGG	ATACGCTCAG	GCCCGGTAAT	GTCAGCGCGC	CAGAGCGGTT
20281	AGGGCACTAT	CAGGCGCAAT	TATTGGCGGC	ATATTACTTG	GCCGCCATCA	GGGAAGTTCT
20341	GAGCTGGGTG	AACGGGCAGC	GATTGGTGCT	ATGTATGGTG	CTCGATGGGG	AAGGATCATT
20401	GGTAATCTAT	GGGATGGCCC	TTATCGGTTT	ATCGGCAGGT	TACTGCTCAG	AAGAGGCATT
20461	AGCTCTGCCA	TTTCCCACGC	TGTCAGTTCC	AGGAGCTGGT	TTGGCCGAAT	GATAGGAGAA
20521	AGTGTCGGGA	GAAATATTTC	TGAAGTATTA	TTACCTTATA	GCCGTACACC	CGGTGAATGG
20581	GTTGGTGCAG	CCATTGGCGG	GACAGCCGCG	GCCGCTCATC	ATGCCGTTGG	AGGGGAAGTT
20641	GCCAATGCCG	CTAGCCGGGT	TACCTGGAGC	GGCTTTAAGC	GGGCTTTTAA	TAACTTCTTC
20701	TTTAACGCCT	CTGCACGTCA	TAATGAATCC	GAAGCATAAC	AATCATGTTC	ATTCCCACTT
20761	TGTCATGGAT	GACAAGGTGG	GTTTTTCGGA	TGTGTGGACA	GAGACCCGTA	CAGGGTCTCT
20821	GTCCAGTTAA	TTTTTGGATC	AAGAACGAAT	GGTGTAACGG	ATATGCAAAA	TGATATCGCT
20881	CAGGCTGAGC	AATAAGCTTT	TCTGTTTACC	ACTGATACCG	GGAAAACTGA	GGGTTAATGT
20941	GCCTGTATCG	GCCACAGGAA	GCCCTTCAAA	TGGCAGGTAC	TTAGCATCAT	TGAAATCCAT
21001	CTGGAATTGA	CCACTGTCAT	TCATGCCATG	TGAGATCACA	ATCGCTTTGC	AGCCACGTGG
21061	CATCATTGTA	CTGCCGCCAT	AACTCAGTAT	TGCCCGGACA	TCCTGATAAG	GCCCTAAAAG
21121	GGCAGGTAAC	GTCACACTGA	TTTGTTTGAT	ACGGCGTGTA	TTACCTAAAC	CGTCAGGATA
21181	ATCGGTAGCA	ATATTCAGAT	CCGATAATTT	GAGGCTGGCT	TGCAGTTGTG	TCCCTTCGAC
21241	GTTCAAACCG	TTAAGCGTTG	TGCCTGCACT	GCCTTCACCT	GCATTGACTA	ACTCAGTCAC
21301	TTTATCTTTT	AAAATGAAAC	TATTTTCTGT	CAGACCAGCA	TACACTTCAG	CCAGAGAAAC
21361	GGTTCTGGTG	ACCTCCAGTG	CCCGTTCATC	TTTTTCCAAA	TAGCTTTTTT	CCATCTGTGC
21421	TAAATTCAGC	ATCAGGGTTT	CACCCGCTAA	TAAACCCGCA	TAAGTCCCAT	GCCAAGCACC
21481	TGGTTTAATA	AAGTGTGCTG	CCGCATTATT	CAATTCATAC	TGATAAGTTT	GCTCTGCCAT
21541	TAAACAGAGT	GAGACCGCCA	AATCATAAAA	CTGATAATAA	ATAGCGGACA	ACGTTCCACG
21601	GAGCCAGTTG	TATAGCGCTG	CATTACTGAA	TTTACTTTGC	AGAAAGGCTA	ACTGCGCCTG
21661	AGTTTGTGCC	TGCTGAGTTT	CCAGATAGTT	TTTTTGTAAT	ACTGCCGCTT	CACGACGTAC
21721	AGCCAGCGTC	GCTAATTGAG	CATCAATTTG	TTTTATCTCA	GCTTCCGCAT	TATTGCGCTG
21781	AATTTCCCAC	TCTTGCCGAC	GGCGACGGTA	TATTTCTGAT	TGGCTGATTT	TGTCTGCGGC
21841	AATACGTGTT	GCTGACGCAG	AAATTTCGAT	ACCAATCGCA	CTGGCATTGA	AAAGCGCCCC
21901	AAAACGGGAA	CCTCCCACAG	CAAAACCGTA	AATATTGGGG	ACGAGATCTG	CCGCGGCGGC
21961	GGCCATATGC	AGGGCTGTGC	CGCTGGTGCT	CAAGACCGAT	GAAGAGAGGT	AAAGATCCAT
22021	CGCTTGTTTT	TCACCAGCGT	TAACATCTTC	GTCGTACAGC	GTATTGAAAC	TGTCAAAACG
22081	AGACTGTGCA	CCATGACGGC	TTTCTTGAAG	CGCCAATTTA	TCAGCATCAA	TTTCAGCCAT
22141	GACCTTATCC	TGCATTTTAA	TACTTTGCAG	GGCTAACTCA	CTGCCTTGAG	TTTGCAGTAT
22201	TTCAGCCAAG	GCTTCTGCAT	CCTGCCGTTC	AGTAATGCTG	AGCAGGGTAT	TGCCAAATTG
22261	TATCAACTGG	CTTACCCCCC	ACTTGGCATT	TTCCAGAATC	ACCGGAAAAC	GGTACATCGG
22321	CATCACTGCA	TGAGGTAAAT	CGCCGCCGCC	TTGTGAAGCA	GTGATGGCAG	CACTGAGTAA
22381	CATGGACGGA	TCTGCGGGCG	TGGCATAGAG	AGATAATGAC	AGTGGCTGAC	CGTCGATTGT
22441	CAGGTTATGG	CGTAAGTTAT	AGAGGCGTTG	CGTCAATGTC	TGCCAGTAAC	CTTGCAGTTT
22501	TTTATTAATT	TGAGGGAGGA	ACAATGCGGT	TAACGAAATT	TGCCGTACGT	TTCGTGGGTA
22561	ATGCAGCGCG	CTGACGCAGT	TGCAGCATTT	TATGTTGATA	ATGATGCCGC	ATTGTTTGGC
22621	TGGCAGCTTC	TTCCAGCCGT	GGCTCTGACC	AATCGTTATC	CAATGAAAAA	TAAGGCTCAT
22681	CACCCAATAA	AGTGAGCGCC	TGTACATACC	ACATTTTAGC	TTCGTTTAAG	GTATCACGTT

BNSDOCID: <WO__ 9808388A1_I_>

Fig.2.

22741	CAAGCTGGCG	ATAGGCGCTA	TCTCCGCGGG	TAATCAACAA	ATCCAGCATT	TTCATAAAGG
22801	TAGCCACTTT	ATAGTGCATC	GGATCATGCT	GGGCAACGGC	GTCCGGATCG	ACCGAATCCA
22861	GCGGATTGGC	ATTCCAGGAC	GTATCTTCCT	CCAATGGGCG	GACGTTCCAG	TAATAATCCT
22921	GCATTTCACC	CTGAACCGAA	TATCCGGTCG	GGTTCAGATA	TAGCGCAGCC	AGCGTGTCGA
22981	TCCGGTAAAA	TCTGCTCTTG	CAATAAGCGC	TGGAATACCA	TCATGGGCGT	TGTAATAGAA
23041	CAATCCCAAG	AAATAGATTG	CATTGGCGCC	GTTTGAAATC	CATGGGTTCA	GTGTTATTTT
23101	TCATGACACG	ACTTGAATAC	CCCTTTTATA	TTTTTTGATA	TTTTTTACTA	TCCCCTGTTG
23161	TGTCATTCCC	GAATCATGAT	CGGCATCATT	AGTGAATATA	AATTGATTTT	TCGTCTCATC
23221	AAAATAAAAG	AAAGCAGATT	CCCAGGATTT	GTCATAGATA	ATTTTTTTGT	ACCCAACCCC
23281	TAATCTGACA	CCTTCACGTA	TGTAATATCC	TTTAGCATAG	GGAACAAAGA	GCGTTACTGT
23341	GGTTTCAATA	TCAGATAACA	TTCCTTCGTA	ATAAGGTTGT	CTGGCAGAAT	TGCCATCAAT
23401	ATTCCCAATA	TGGATCTTAA	ACCAACGTTC	ATCACCATGC	TCCTCTTTAT	TGTAGGGGGG
23461	CAACTTAAAT	GTCGCATAAA	ACCCTTCACC	TAATTGCGGC	TCTGGTAAAT	TTTGCGTTTC
23521	CATACTTAAA	ACATTATCAA	TACCAATATT	GGCTCTTTCA	GCTAATTTTC	TGGAAAATAA
23581	AGTATTTAAC	CGGGTTCTGT	AAGGGCCAAT	CTGCATATAT	TGTGTGCCTG	ATGGCATTTT
23641	ATGCAGTGAT	ATAACGTTAC	TTGTATCTTT	GGATTTTAGT	TTTATATGAA	TTGGCGATTC
23701	AATAACAATA	TCGTTATAAC	CGCCGTCGGG	TTGCTTAATA	ATAAACTCGC	TCACCAGAGG
23761	AATATCATAG	CCTTCAATAT	CAACTTTTAC	TTGATTAAAA	TCATATACCA	TAGGGTCAGA
23821	TTCGTGTGAA	GGTTTAGATG	CCACATGGTC	TTCAGCATTT	AACTCCACTA	GAATATCAGA
23881	GCCATTTTTT	AATAAAAAAC	TAATGTTTTT	ATCTTGGATC	TGTTCGATCA	TAGATGAAGC
23941	AAGTTTTATT	ATCTGTGGCT	GGTTGAACAT	AAATACACCC	ATGGATCCTC	GCGAAGGAAC
24001	AGTGCCGCAA	TATTTCCCAT	GTTATTAATG	ATTGAAACAT	CATTAGTAAA	TGATTCACAT
24061	ATAGTATGCC	ATACTCCTGT	GTTATCTTTC	CAATCTAATA	CTATGTTAGT	ATCAAGTTTG
24121	AATTCAGCAT	CATCTGATTC	ATAATCATAA	TTTATACCAA	CTCCAATTTC	TGATTTTCTA
24181	GGAATTTTTT	CCTTGGTTCT	TAGATGCATT	AACACTCTAA	AATATTCGGC	ATTTTTAAGA
24241	TCGATGGAAA	TAATAAAATC	CAAAGTTCCA	TAATGAAAAA	CTTCTTCTTC	TTTTCCAAGC
24301	ATTTCATCAT	GTCTATCATA	ATCAAATAAA	ATAACCGTTT	CATCTTCTAC	CATCGATAAC
24361	AGGTATTTAA	CCTCATCATT	ATATATATTG	CCTTTTGAAA	AATTAATTTC	CATTGAAGGA
24421	TTGAACGTTA	AATTAATATG	ACCATTTCCT	GGTGATATAT	ACGAGAGATC	AAAAATATTT
24481	CCGGTAAAAC	TGGCTAATTT	ATTTTTTGTG	GTTATAGATT	CCTTATATTC	GGCCAAATAA
24541	TCTGTAGCAA	ATTGATTGTT	GACTTTGTAT	TCTGTCCTGG	TATCAAGTTC	TGATAATGTG
24601	CTCTTAACAA	TGGCGTCTAA	ATCATTTTCT	GTGAGAATGG	ATAATGTCAT	ATCAGGGTTA
24661	ATGGTCATCC	CTTCTCTTGC	AGGAAGACTA	TTAAAAGAAT	AATTGTCTTT	TTTCTCATGG
24721	AAATAAACAA	TAATGACGTC	TTTTTCATAA	TCAGAAGAAC	AATACATACC	AATGCTGGCT
24781	TTTTTATTGA	TCAGGTTTTC	TATTTTATCA	GTCACATTAA	AATTAAACGG	TGAGCTCCAG
24841	CTGCCATCAT	AACGAATATG	TGACAGTTTT	AATATATAAT	CAGTGATATC	TATCTTGCCA
24901	TCTTCACTTT	CATTTTTCAG	CTCTTTTTGT	TCCAGCCACA	GTAAATACAA	ACGAGACTTG
24961	TAAATAACAG	GTCTGATATT	TTCCTGCCAT	ACATTGATGG	GTATTTCAAT	TTTTTTCCAT
25021	TCTCCCCAGG	CATTGGCAGC	AAATTGACCG	TGCTGGCACT	TTTGGTGATC	GACATTGCGC
25081	CAATAATATA	TTCTGGGTTC	TGTCTGGCTA	TAACCAATTA	AATAAGTGAG	CCCCTCATTG
25141	ACATTAATAC	TGTCATGATA	TCCGCTAATC	ACCTGCAAGT	TAGCGACATC	TTCAAATGCG
25201	GTCAGATAAT	TTTTAAAGCT	ATCTTCAACG	GTATCGATAT	TTAACTGACT	TTGGGAAAGT
25261	TGCTGTAACA	GGTTGTTCAT	CATACCTGTC	TGACCAATAC	GAATCGTGGG	GTCGATATAG
25321	TTTTCCGGAT	AATAGGCCAG	TTCAGATACG	CCGGCCCAGG	TGCTATACCG	TCGATTGTAG
25381	GTTTCCCAGT	CGCAGAAGAA	CTGACGGGTT	TTCACTGGCT	TTGATACTTT	TCCTTCAACA
25441	TTATTCAACG	CCCGGTTGAC	ATATAACTGA	ATGCTGGCAA	TGGCTTCTGC	CACACGGGTG
25501	GTTTTCACTT	GGGCAGAAAC	TTGGTTATCA	ATCAGCAGAT	AGCTGTACAA	CTCATCCCGG
25561	CTCTTAATCT	GTTGAGGTGC	ACCATTTTTG	ATGTAGTAAG	CACTGGCCGC	TGTCGTCGTG
25621	GCTTCATCCA	GCCATGCCTG	AAGCTGGTCG	GATTGTTGAC	TGTTCAGTCC	CGCCTGCAAC
25681	AAAGTACTGG	CGGCTTGCCA	ATCATCAAAT	GTTGGCATCG	GGGTTTCCGG	TTCACCGACA
25741	TATTTTAATT	TTATGAGTGC	AGCAACACCA	TCCGGGGTAA	TACCCAATGT	AGCAGCGACA
25801	TCCAGCCATT	GCAGAGTGAC	ATCTATAAGT	TCTCCAGTTG	GTAAAGGTAT	TCACTCCCAA
25861	ACCGGTCTGT	TGCAATGCTT	GTGTCACAAC	CTGAGCATCA	AAATTTTAAC	GCCACCGCCA
25921	AATTGTTCGG	CAGTCAACGC	TCCTAAGTTC	CAAATGCTGT	TAAGATTCTG	TCGCGTAGCT
25981	TCACAACGCA	TGATCACAGC	ATGGAAGCGG	GTCAGCGCTT	GCAAAGTGGG	GAGATCATGT
26041	TGCAGTGCTG	TGGTTTCTGA	TTGGAATTTC	TCCGGTTTTG	TCACCAACAG	GGTCAGTTCG
26101	TTTTCGCTGA	GTCCAATATT	GCGCACAATC	AGAGAAAGTT	GCCCCAGTAC	CTGACAAAAA
26161	GCCACCATGT	TGCTGGTTTC	ATTCTCTGAG	CGATCACGGT	TAGCCGCAAT	AATCATGAAA
26221	TCATCGAATG	TCAGTCCTTG	TGGTTTTATC	TGATTAATCC	ACAGCAAAAT	AGTTTCTGCT
26281	GTTTTGGCTG	AATCCATTTG	AATGCTGGCA	GCAATCAGCG	GGGCAGCTGC	ACGGATCAGT
26341	TCGTCATCAC	CGAGTGAAAG	TGTTGATAAT	CCATTACTTA	GTGTCGTGAT	AAGGTTTTCA
26401	ATATCCGGCG	TAAGGACAGT	GCTGTAATTA	TCCGTGGTCA	TCAGAAACAC	ATCACTGACA
26461	GACCATTTCT	GTGTTGTCAG	CCACTGGGTG	CATTGGAACA	GAAAGCTGAT	TAATTGCGTT
26521	AATGCTGTAT	CAGAAAAAAG	GGCAATTTTC	GTGTTCACAT	AGGGAGAAAC	CGACAACAAC

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Fig.2.

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26701 CATAATGTAT ACAGTTCAGT ATCATTCACT CTGAAAGCAC GTTTCATTAT TCCCAAATAA
26761 AAATGGTTTT TTGATTCACC GGGGGTTAAA TCCAGTTTGG TATTATCAGC AGAAAACTCT
26821 TGGCCATTTA ATAGCGGTGT ATTGAACAGC ATTGTAAAAT GACTGGGTTG TTGTTTAGTG
26881 GAATATTGGC TGATATCTGA ATGACACAAT ACCAGCGCAT CGCTGACGCT AATATTATAG
26941 TGCTGCATAT AATATTGAAC ATAAAACAGC TTACCCAACA CATTGCTGTC AATGGTTAAG
27001 TCATCATAAA TACTTTCTAT TACTTGCCAG ATATCTTCTG GAGATATGCC TGTGGCTTTA
27061 TACAAACGAA TCGCTTTATT CAGCTTTAAC AGGAATATAT CACCGGGAAC TCCATCATTT
27121 TAAAGTGTGC ATTGGCATTG ATAGCATCCG ACGGATTTGG TTAACTCGCC ATAAGCGGAG
27181 TGTTATACCG TTGGTGATTT GCTCTGTCGT CAATTTAATG GGAATACTGT AATGGGTATT
27241 AGCAATGGGG ACGAAATTTT TATCTTGGTA TATATATTCT TTATCTCCAT TCTGGAGACG
27301 AAAATCCAAG TGGTCAGGTT CTGTTTTTTT TACACTGAAA TTATATTTGT ATTCATTTTC
27361 TTTGATTGGA ATTAGCTCTG CATAGTTTAA ATGTGAATCG TAGAAATCTT TGCGGGTTCG
27421 CTTAATCAAT CTTGCCGTTG CCGTATCATT CCCGTCATTG ACCAATGTTA TCAGTTGCTC
27481 ATTCTTATAC TGTTGATTTG TATTTTTCTT ACCGAAGGAG AGATTGACAA ATAAACTGAG
27541 TTCATCATAA GACAAATCGT AGTAGCGAGC CAAAGAAGCA TAACTCTTAA AAATCAGTAC
27601 ATCATCTGTA CCGAAATTTT TCTTCATCAG TTCTGTTGAA TTTTCCGGTG TAATTTCTTC
27661 TACAAGGATT TGATACAATT CAGGCGATAT ATCAGTCTTA ATAGCCAGTA GCGATGTTGG
27721 GTCCATTAAT TCCGCTACGT CTGTATTACG GCTAAATGCG GTGAGGTTTT TATCTTGCAA
27781 TAAAATTGCC TGACGGGCTG ACTCATACGG CAGATGATAG GGTGTCATGC CGGTTTGCCG
27841 GTAAGTGGAC AACATTTTCA TTACACCGTT ATAGTCAGTT TTCTCTAACG TCTGAATATT
27901 ATGCAGCAGT AATTCATTAG ATAAGGATAA TGTGGAAATT TCTTCATCCA TATTATTCTG
27961 TGTCAGTGCC AGTGAAGCAA TGTCGGGGCG TCGTTTATTC AGGTGATATT GAGAATTGTC
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28201 AGCACGGGAC AAAATGCGCA GTTCTTCAAG TTTATTCTGT TTTGATTCCT GATGAGCCTG
28261 TTGATATAAA AAGTCTGTTT CTCGCCACGT CAGAGTTCCA CTTGTCCTAT GACGAAATTC
28321 GCTGAAAGAC ATAAACGAAA TGTTTGTCAA TAATAAAGTA TCACCAGCCT TTTTCTATTT
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28861 AACCTCGCAA ATGCGGGGTT TTTCTTCGCA TAATCAAAGA GAAAGCTATG AAAAAAACAC
28921 TGATTACTCT TATTCTCAGT ACCCTTTCTT TTGGTGCTTT GGCACAGCAG GGTGGCTTCG
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29041 CCAGCGTTGC TCAAGCAAAA TCTTTTCGTG ATGATGCGTG GGTTGTTCTG GAAGGAAACA
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29641 CCTTTAAACT ATATTCGGGG GAAATTATTA TGTCAGATGT TCGTAATATT ATTAATGTTG
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30001 GCAATAGTTA TCTAAAATTA ACGTGATGGT TTTGGCATTA ACATATTGAT TGTTAATTTC
30061 ATCTAACAAT TTGATAAATA AATCTGAGTT CTTTCTCAAG CTACCGACAT AAGTGATTTC
30121 TTTCGTTTTC GCGTTGAGGC AATTGGCAAG GTAGTGTTTT TGGTTCTTTC CGGGGGTAAC
30181 AACACGCTTT TGTTGCCCTT TGAAGCACCA GTCTGCACCG ATTTTCGGGT TCAGGTTGAT
30241 GTCCACCTCA TCCTCATAGA AGACCGGGTG TTTCTCTTGA GGCATTGGAT AACGTCTCGC
30301 TGATTTTTGC CATTTTTTCA TCATACTCAG GGTCAGGCAA TTTTACGGTT GGTGCCGCCC
30361 TTCGCCAAAC GATGCCCGTC CGGCAAAAGT AGCGATAGAG GGTACTTTGA GAGAGCGATG
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Fig.2.

30421 TATTCAGTAG CTCATTGATT TTAAGTGTAA TAAGCTCAAG GCTCCATCGT GAACGGAGAT
30481 AGCCAAAATG TTGTGGCGAG TGCTGTAATA AGAAAGAAAT GACTGTGAAG AGCGGAGCTA
30541 AGTTCCAGAT GGCAGGCCTT CCCGCCGGGA GGCTTTTAAG TCCTTCCAAC CCGTATAATG
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30721 TATCCCGGGT TTTCTGGATA GCTTTTTTCA TCGGACGTCG TTCATTTCGG GGTATTGATG
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30841 CGCGAAAATC GGACTGAGTT CCCTTCAAGT GATCTACTAT TTTGAAATCT TATTTAATCA
30901 GGAGTCAGCA AATGAGTTAT TCCCCATAAT ACCTGACCAT GTGGTTGTTT ATCCGGGAAA
30961 TGATTCATCT ACCGGTGGTA TGTGGATTCC TTGGTGCGAT AGTCAGAAAG ATATTGACTC
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32341 TTTGTCCATC AACTGACTGA ACAATCTCCG GAGCATGAAA CCATGTTGAT GACTATTGCA
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32521 AGTCTGGACA TCATTGTCAC CAGTACCGGC CTGAGCCGGG AGAAAATTGA AGCGTTAAAG
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32641 ATTTTATTTA CTACGATTTA CGACGGTTA CTTTAGGAAG CTGAATGAGA CGTCCTTTGT
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32821 CCAATTTCAT TTTGGTTGCA TAAATTCCCT TATGCAGCAC AGTGCGGGGC GTATCCAGTG
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32941 CCAGTTCAAA CTGATTTTTC CCGCGTGCAA TTTCATATTC CGCATCGTAT TGGTTATTCA
33001 GCAGACAGAA GAATTCCGGA GCACCTTTTT CCATCGTGCC CAGTGGCTCT CCTGTTCTGT
33061 TATAGCGGCG CGTTGTCAGA TCAGCACCCA GACATGAACG TCCATAGTTA GCAAATCCGA
33121 GGTGAATTTT CTCCGGTTGT ACACCTTGTG ACAGTAAAAA GCGGATCGCC TCATCTGCCG
33181 AGTAATCCAT GTCCCGATCA GGATTGGGCG GAGGAGGGTT ATCGCCGTCA TATTCATATC
33241 TGGGGGGATA CAGGTTAGTA TGGTGACCGA TGTATTCTGC CCAACCGGTA CCAAAGAAGT
33301 CGTAGGTCAT CACAAAGATA TTGTCTAAAT AAGGTGCGAT TTCTTTGAAG CTGGACTTCT
33361 CCATTTTGGC AACGACGGCG CTACAGGCTA TCGTGATTTC TTTACGGGCC CGGGTTCCAA
33421 AGGCGATGTT CAGTGCTTCA CGCAGCTCTT TCACTAACAA AACATAGTTT GGGCCATCAT
33481 GTTCCGGGTC GAATTCATTA CCTTCTTCAC CTGTGGCGCC GGGGTATTCC CAGTCGATAT
33541 CCACCGCAGT AAACATGGGA AAACGCCGGG AAGAAGTCGA CGATGCTACT CACAAATGTA
33601 GCACGTTGCT CAGGATCTTT GGCCATCACA GAGAAATACC CTGACATACT CCAGCCGCCG
33661 ATACTGAATG CGAGTTCCAG CTTATGCCCT GCCTGTTTTG CTCGCGCTTT CAGATTACGC
33721 AATCCCCCCA GTAAACCGGA GGCTGCATCC TGATTGTAAT ATTGCAAGAA ATTCTTCGGG
33781 CTGGCATCAC GGCGCTGATC CGCGTCCAGA CCGACATTGC GTGTGGTGCC TAAATCACCA
33841 TAAGGATCAA CGGGTACAAT ATGGCCTAAT GTAATAGGGG CAATCTGGCC ACTGCTGGCT
33901 TCTGCTTGCC GGTTCCACCC GTCAACAACC TCATTAATCC GTTCGGATAA CTTGCCTTTG
33961 TCACCGTTGA CGGCCATAAA ACTGAAAATC AGGCGGTCGT AGGCGGTAGG CGGGATTTTT
34021 TCCAGATCAA AACCACGGCC GGGGGCATCG TCGCTGGTCA GCGCAGTGTT ATCCTGGGTT
34081 TCTGGCGACA AACGCGCATC ATACTGGCAC CAGTCAGTAA TATAGGCAGA GACTTTAGGC
34141 AGCGGTTCTG TATTTTCCGG ATCAACTTCA TATTCGTTGT ACAGGGACTT GGCAACACGT
34201 GCTGAAGAAT AACTCAAAGG AGTTCCGCTG CCGTCAGGTT TATATCCCAC CTTCTGATAG

SDOCID: <WO___9808388A1_I_>

Fig.2.

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34261 GTTTCTTCTG TGAGTGCATC ATATTGCAAT ACCTCGGTTT TTTCTCCCGG CGGTACATCA
34321 GGCGTATTGG GGTTACCGTG ATCGGCAATT TCTTCCGGTG TCGCCTCACG GACATATTGC
34381 CAGGCATTCT CATAAACCGG TAAATCAGGT GAAATATTGC GGTCGGGAAT ATGCCAGCGT
34441 TCAACCCAGC CGATGTTTTT AAAAACCGCG CTATCATAAA TGACATACCA GGTTTGACCA
34501 CCAGATTGAT TCTGCCAGGC AACCAGAGAT GCGCCTACTT CGCTGCTGGC GTCAGACATC
34561 GCTTTAATTG AAGGGTATCG ATAAACATTT TGAGACATAA TTTCACTTCC GGCCCCGTTA
34621 TATTCCGGGG CCGGCTCCTG ATATCAGTTA GAATTGTCTT GTTTTAATTG ATGTTTATTC
34681 AGACGGCTAC GAACCTGCTG GCTGAACTCA TTACTTCCGC CACTCACATC ACGCGCGGTA
34741 TAACGCAGAT GGAGGATAAT ATCGCTCAGC GACTCCAGCA GCTGATCCTG ATCGGAACCG
34801 AATTCCAACT TCCACTGTGA AATGGCGCCT GTCCCTTCAA AAGGCAGGAA AAGTTCATCA
34861 TCAAAATTGA GCCTGAACAT GCCGCTGTCT TCCATGGCCG TTGAAATCAC CACACCTTGA
34921 TTAGCCTGTA CGTTCAGCAA AACGTTTTCG GGTTTGGTGT ATTCCAAGGG GTTAAGCAAA
34981 TAATCGATAG TTTTTAAGTC AGCAGTACTG TAAAGCGTAT TGCTGAGTTG TACCAGTGAA
35041 GCCCGTACAT CTTCATAAGG CCCCAGCAAT GCGGGCAATG ACAGCGCTAC GGTTTTTATA
35101 CGCCGATCAG CGTGGGTCGG ATAATCGCGC AAGAACATTT CGGCGCTCAG TAAGAAAGTG
35161 AATGAACCCG TACTCTTGCC AATTTCCCAC TGTGATGATG TCAGTAATGA TTTTACCGAT
35221 ATGGTTTTTA TGATCTCCAG ACGTCTGGTG TTATGTTGCA AATACGCCTG ATCCATCCGT
35281 TGTAAGGCTA ATTTCAGATG TTCTCCGACC AGCAGCCCCT GATAAAGATC ATTCCAGAGA
35341 CCACTTTGGA CGAAATTCAT ATCATACTGA CCTGTTTCGT ACTGCCAGGA GGCTTCGGCC
35401 AGTAAACAGA GGGAATTAAC CGCATCATAG GCTTGCAGGT AAAGCCGGAG ATTTGGCTGA
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35881 GTGCTGCCGT ACTGAATCAG CGTTTCTGCG GCCTCTTTTG CCCGGCTCAT GATCGGGGTG
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36421 TCTAACAGAT TCTTGACATA GAAACGGAAT ATTGCTTTCC GGTAGTGAAT GGGTTCACTG
36481 GCTGCAATGG CATCCGGATC GGTTGGTTCA ATTAACATCC GGTACACGGT GGGTGGAGGA
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37561 TGAAGACGGA CAAACGGAAC CAGAGCCAGA AACGGGTTAT GCGGGTCTTG CTGTATATCC
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37741 AGGAACCCAA TCACCCGCAC TAGGCTCAAC GTTTTGGTTA TGCAGTGATA ACGCAGTTGT
37801 ATCTTTAGTT TCAGACTGTT CTTCAACTTC CGTCCAGGCA ATATACAGGC GATTATTCAG
37861 GAAAATGGGG CGTATCAAAT TGGGGTCTAC GCTGCCCAAT GGCAGGTCAA TAGGTTTCCA
37921 CTCGCTCCAG GCATTGGGAG ATAACGCATC GGTATCAGGA TGGCGTATCG AAAGATTCAG
37981 TGAACGCCAG TAATATTGGT ATGGCTGTGT ACGGGTACGT CCGACAAAGA AGAACTTATC
38041 GCGTTTGATG TTAACACCAT CTTCATAACC TGCGATAACT TTCAGGTTAC TGACATCTTC
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Fig.2.

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38101  AAAATTATTC AGATAACCGA GCACCGCTTG TTGTACAGAA TCTTCGGTAA TTTTTCCCTG
38161  ATTAAGGGCA CTTTCCAGTT GGAAGAAGAA TTCTGTTTTA TTCAGGCGTA ACAGGGGTTC
38221  CAGATAGCTT TCCGGATAAG TCCGTAATAA GCGATCCC
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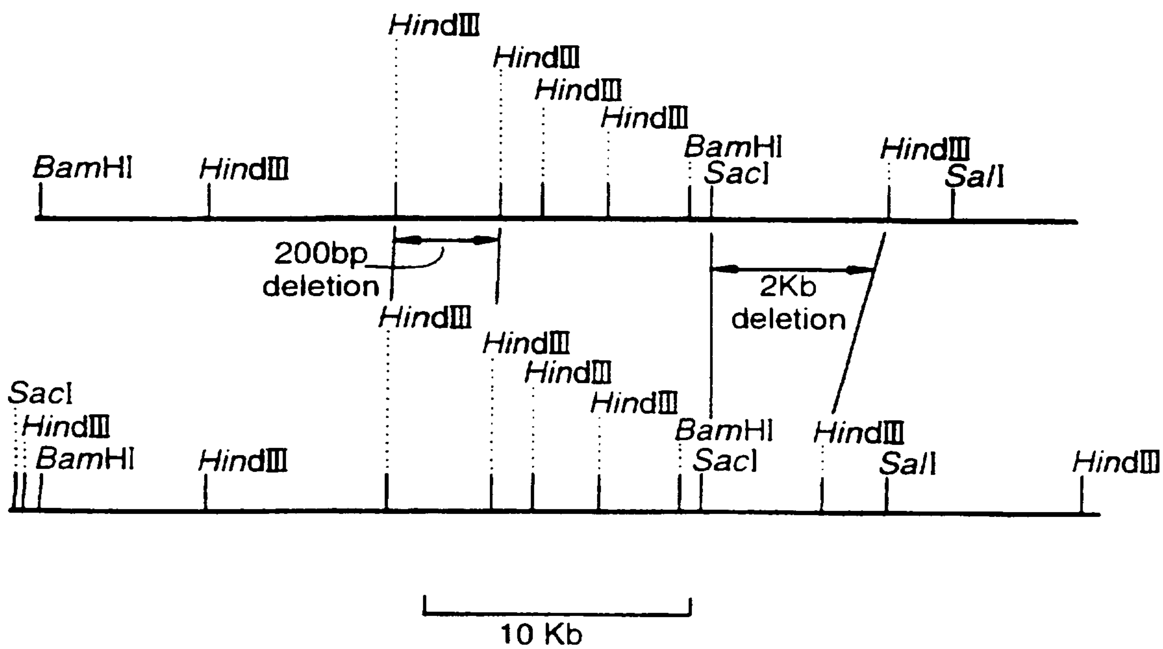
N=unspecified base

Fig.3.



INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 97/02284

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A01N63/02 A01N63/00 C12N1/20 C07K14/24 //(A01N63/02, 63:02,63:00),(A01N63/00,63:00)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 00647 A (COMMW SCIENT IND RES ORG ;SMIGIELSKI ADAM JOSEPH (AU); AKHURST RAY) 5 January 1995 cited in the application	1,5,11, 13, 18-21, 24-26, 29,30,32
Y	see page 1, line 3 - line 29; claims 10-13	3,4, 6-10,12, 14,27, 28,31

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Date of the actual completion of the international search	Date of mailing of the international search report
17 December 1997	14/01/1998

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	CHEMICAL ABSTRACTS, vol. 118, no. 1, 4 January 1993 Columbus, Ohio, US; abstract no. 3550, YAMANAKA, SATOSHI ET AL: "Biochemical and physiological characteristics of Xenorhabdus species, symbiotically associated with entomopathogenic nematodes including Steinernema kushidai and their pathogenicity against Spodoptera litura (Lepidoptera: Noctuidae)" XP002048914 see abstract & ARCH. MICROBIOL. (1992), 158(6), 387-93 CODEN: AMICCW;ISSN: 0302-8933, 1992, ---	3,6
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INTERNATIONAL SEARCH REPORT

national Application No
PCT/GB 97/02284

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	H.MATSUI ET AL. : "Nucleotide sequences of genes encoding 32 KDa and 70 kDa polypeptides in mba region of the virulence plasmid, pKDSC50, of Salmonella choleraesuis " NUCLEIC ACIDS RESEARCH , vol. 18, no. 8, 1990, pages 2181-2, XP002050055 see the whole document ---	21-25
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International Application No
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(74) Agent: SKELTON, S., R.; D/IPR, Formalities Section (Procurement Executive), Poplar 2, MOD Abbey Wood #19, P.O. Box 702, Bristol BS12 7DU (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: PESTICIDAL AGENTS

(57) Abstract

A method for killing pests (e.g. insects) comprising administering material from *Xenorhabdus* species (e.g. *X. nematophilus*) such as cells or supernatants orally to the pests, either alone or in conjunction with *Bacillus thuringiensis* or pesticidal materials derived therefrom. Also disclosed is an isolated pesticidal agent (and compositions comprising the same) characterised in that it is obtainable from cultures of *X. nematophilus* or mutants thereof, has oral pesticidal activity against *Pieris brassicae*, *Pieris rapae* and *Plutella xylostella*, is substantially heat stable to 55 °C, is proteinaceous, acts synergistically with *B. thuringiensis* cells as an oral pesticide and is substantially resistant to proteolysis by trypsin and proteinase K. DNA encoding pesticidal activity is also disclosed.

*(Referred to in PCT Gazette No. 29/1999, Section II)

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ML	Mali
MN	Mongolia
MR	Mauritania
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NE	Niger
NL	Netherlands
NO	Norway
NZ	New Zealand
PL	Poland
PT	Portugal
RO	Romania
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SI	Slovenia
SK	Slovakia
SN	Senegal
SZ	Swaziland
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UG	Uganda
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VN	Viet Nam
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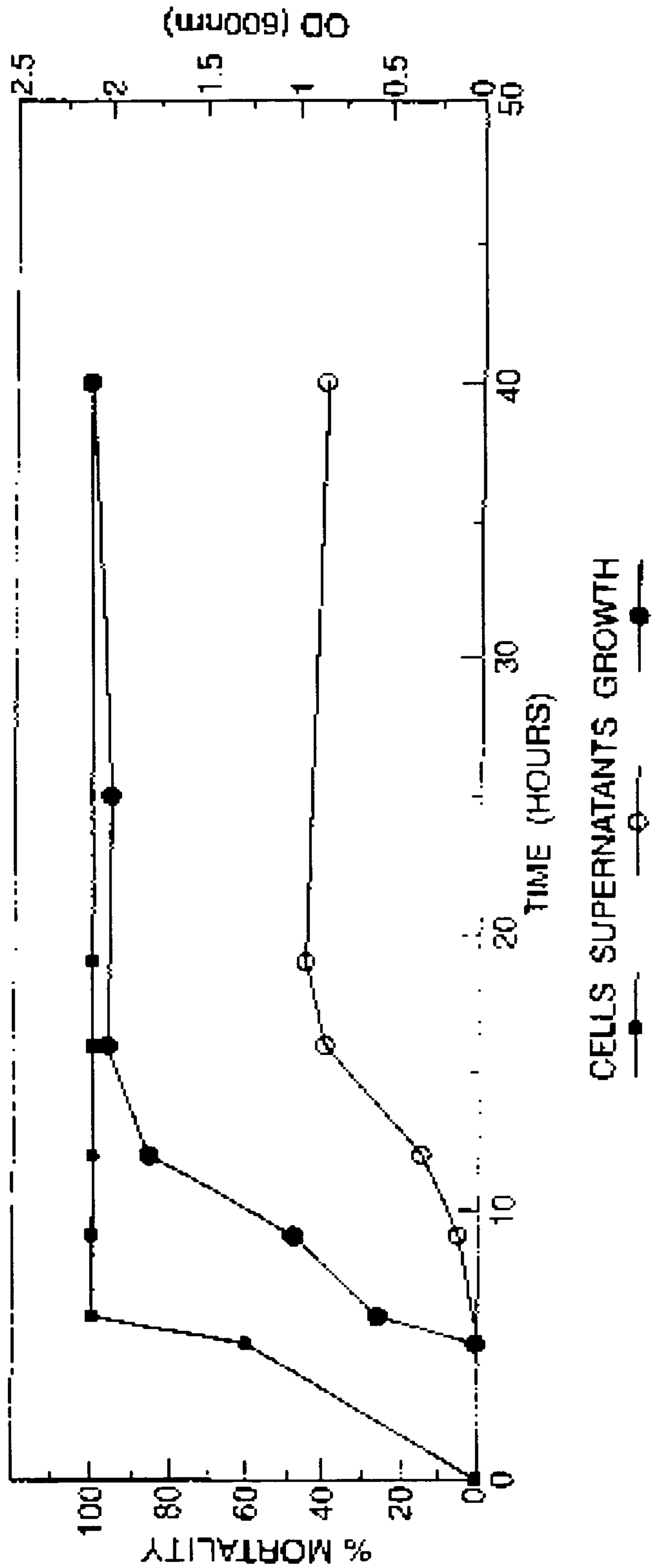
ZW	Zimbabwe

Fig.1.



SDOCID: <WO _9808388A1TI_>

Fig.2.

1 TCCACAATTG CCGGAGAAAA TCAGTCGGGA ACTGCCGGTG ATTATTCGTC ACTTATTAAA
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181 TGTCAATGAT ATGACCGGAA TGAAGATGGG CAATAAAAAC ATTAGCCCAC GAGCACCGAG
241 ATTGTACTTG TATCATGCCT ATCTCTCTTT TATGGAAGCG CACGGCTTTG AACGTCCGTT
301 AACACTGACT AAGTTTGGTG AATCCATCCC CAAGATTATG CTGGAATACC GGAAGGAGTA
361 TCGAAAAGTG CGAACCAAGA AAGGCTATTC CTATAACGTG GAATTATCGG AAGAGGCCGA
421 AGAATGGCTA CCGTCAGTGC CTGAGTGTCG AGACTTTAAA TCACCTGTAT AAAACTTTGA
481 GCTTTAAGTC TGCACTCCAT ACACAACTTA AAATATCTAA TTGTATTTAA AAGAAAATAA
541 TAGATGTATA GTTATTTTTT AACTATACAT AAGCTCTACA TGCTCTTCAT TCGTGTAAAA
601 AATGGGTGAA CAGGTGATAC AGTCAGTGAA TATCATATTA ATTACCGTAA ACCCAGATGT
661 AGCAAGGCTT TCAGGGAATT GTGCAGAGGG TGCATAACTG AGAGGGTGAA AAAGATTTTC
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781 ATTTTTTGGT ACTACCTCAA ATTAAAATGA TGTAATCATC TGATTTTATT TAAGAATAGA
841 AGTTAATCAC AATTTCATTG ATGGACTTTC ATTCACACTG GTATAGATAA ATAATTCTGT
901 TATATCCTGT TTCATTACGC ATTCATCAGG AGTGCTGTTA CAGGAGACAA GAATGTCACA
961 CATCATTTAC TTGTCGTTAA AGGGCAAGAA GCAGGGTTTA ATTTCAGCGG GTTGTTCAAC
1021 GCCTGAATCA ATTGGAAATC GCTATCAAAA AGGACGTGAA GATCAAATAC AGGTATTGAG
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1141 ACCCATTGAT AAATCCTCTC CCCTGTTTGC TGGATGCCAG TTTTGTGCAT TACAGGACAA
1201 GCCAGATGGG ACAACTGGAG TTCTTTTATG AAATCAACCT GACCAGTGCC ACGATTGTGG
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1321 GTGATGCTCG ATTATAAGTC CATTTCATGC AACCACATCG CCGCAGGACT TCGGGCTACA
1381 GCATACGCAA TTAGCCGGAA GTGAAGAAGC AAGCCGCTTT TATCTGGGGT CTCGAATGTT
1441 AAGCCACTTA AGAAGCCGCT GGTTGAAGAA ACCCCGGTAA AACCCGCTAA ACATCATGCC
1501 CGTTATCGTT GTGTGGATGA TGACGGCAAT CTTTTAACCG AACGCAAGTA TCGGGTTTGC
1561 CTGCCGGATG GTCAGATAAA AGAAGGAAAG ACTGATAAAC AAGGTTACAC CCAATGGCAT
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1681 CTATACCGTT CAGACAAAAA TAGAATCCAA CGTACCTGTT GAAAACCTGC TTTACGACTT
1741 AACCATTTAT CGTAAGGATG CAAAAGGAAA TTTCCATATC TTGCTTGATG TTTTTCAGGA
1801 GAAACTACAG AGTAATTATG AAACACAACA GCATATCACC CAGGAAATAG ACGACGATCT
1861 TTCTGTGATT TATATTATGC AAATTATGCT TCACCGCAAA CATGGCTCAA ATATATTTCC
1921 GGCACTGCAA ACCCATTTTA AGAAAATGTA TACCCTCGCT GAATTAACTT CCCGTAAAGC
1981 CTGTTCGGAG AAAAAACGGG AAAATGCCTC TTATTTTGAA AGTACAGTTG AAACAAAACC
2041 TGTCAGCGAC GGGGATAATA CCGTTGACTT AAATATCACT ATTCCTGAAC GACCTTTTAT
2101 TGCCAAAGAA TATCCCATTG GTCACCCACA CGATCCATTT GAAAAAAGTA AAATTGAATC
2161 ATAAATACAG GACAGGTTAT CGAAAAGAAT TTATCCGGAT CAAAATGGAG CAAGTTTATG
2221 TCAGGGCGCG AGCACACTAT TTTAGCTGCG TTTTTAAGAT GATTATCTCT TAATCTTCAG
2281 TTTTAATAGT GTTTTTATCG AGTGAAATTT AATCGCACAG GCAATTCTTT AGACTTTTAT
2341 AGAAAACTAA AGAATTAAAG AACAAGATTC ACATTTTAAG TTCAAATATT AATCAAAGTA
2401 TGCTCGCGCC CTGAGTTTAT GTGGCCCTGC CGCTTTTTTT TATTGCCTGC CAATAGATAG
2461 ACCAGATATT TATGAGCAAG CGGCACGAGA ATTATGGCAA TATGGCCGAA CTAAAATTGG
2521 TCAACTGGAA ATTAAGCCGG GTGAGGGTTG CCGACATCCT AAAGGTACTT TTTATAATCA
2581 ATATGGTGAA AGAATATCTG GGTTAGATTG GCTGACATTG GCAAGCCTAA GAGATTCAGA
2641 AAATATGATG ATGAGGTTGA TGATGAAGTA GCTGGTATTA CAATGTGGGG AAAATTGACA
2701 GAATGGTTTG AAAAATCAGG GTATGAAAAA GTATTTAGTA ATGTCGGCTT ATCCCATTCT
2761 AATATAAATG ACATAGTAAC TCTTAGTGAT TACTATAACA AAGGATATCA TGTTGTTACT
2821 TTGATTTCAG CAGGAATGTT ATCAGATTTT GGTGACATAG AAACATCAGG AAAAAATCAT
2881 TGGATAGTTT GGGAAGGAGT AGTAGAAAAC TATGAGAAAG AAAATATCAC AAATAATTCA
2941 GATCTGAATC AATATGTAAA TTTAAATCTG TTTTCATGGG GTAAAGTGGA ACATCAAATT
3001 AAAAAAAACA AATCACTAGA TTATGTACTC AACCATATTT TTTGAGGGTT GGTTTTTAAA
3061 CCAATGAAAT AACATGAAAA AAATATTAAT TATTTTTATT TTTTTACTTT ATGGTTGTGG
3121 TAATCCAACG CCAAAAGTTT TACCAAAATC AGAGTTTCTT CCTGATGCAG TGATAAATGA
3181 ACCATATCAG GCATCAATTA CCATCACAGG AGGTGCATTG AATGAAAAAA GCGTTTGGGT
3241 AAAAATTCAT CCTACTGGCT CAGGACTAAC ATGGAATCCA AAAGATAGTT CTTTCCTATA
3301 GGGTGGAAAA AAAGAAATAA GAAAAGATTA TCATCATATA AATATAACAG GTACCCCAAA
3361 GAAGACAGAA TTGATAAAAA TTGAAGTGGT AGGATTTACA TTGGGTACAA TGTACGCACG
3421 GAAAGAGTTC ACTATAAATT ATACTATAAA AGTAAGGGAA TAATTGTCAC TATCAGAATG
3481 GTGATTTAAT TCGCCATTTT TATACTTTTG TATACTCTCT CAACATAATC AGGATTCTTT

BNSDOCID: <WO___9808388A1TI_>

Fig.2.

3541 CTTATTATTT TTCATGGTGC TAAAAACGTT TATTGCAAAA ATAAATTAAG TTAATCAGAT
3601 AAATTATCTG CATTACTGTT ATAATCGATA ACACGATAAC CTGACTTTCT GCCTGTTCTT
3661 ATGAACTCGA AGATAATCCT TTCTGAGCCT GAACGAATCA CATTGCAACC ACTCGCTTTG
3721 AATCACCCAC ACGGGACAT TCGTACGCGA GGAACGGGTT TACTCATGCT TGCCAGAGGG
3781 AGCAAGCCGT CCCAGATCAC CGCTGAAATC GGATGCAGTC TCCGGGTTAT CTGTAATTGG
3841 GTTCACATGT GGCACAGATA GCGGGATTAT TCGGCGGTCA TGCCGGAGGC CGGTATCTCG
3901 CCATGACGCC TGACATGATT GCCACTGCGC TCGAAGCCGC CAGCGCAGAG TCCCTGACGT
3961 GCGTCGAAGC CAGGCAGGGT TTCCCTGCCT TGTACGCTTG AAACGCTGGC GAATACCCTG
4021 AAAAAACAGG GGCTCCCCTA TAAACGCCCC CGCCTGTCGC TTAAAAAAAG CGCAATAAAA
4081 CGGAGTTTGC TGAAAAATCC GCCTTGCTGA ATAAAATTAA GGCCGGAGCA CAGTCAGGAC
4141 ATTACCGTCT GGTCTATTTT GAGTTCTGGG GGCGTTAAAT TACACGGATA ACACGCTGTT
4201 TTACCAGACA ACGTCAGGCA GTATCACGCG AGATGACGTG ATTGATTTTT TAGAGCCGGT
4261 GGCCAGACAA GGGACAACCG CCTGACATTT TTAGTGTTGG ATAATGCGCG TATCCATCAC
4321 GGGATAGAGG AAAAAATCAG AAATGGCGGG TGACGAGAAC ACAACCTGTT TTTATTCTAT
4381 CTTCCCGCTT ACAGCCCAGA GCTGTATCTG ATTGAAATCG TCTGGAAACA GGCCAAATAC
4441 GACTGGCGAC GTTTTATCAC CTGGACTCAG GATACAATGG AATATGAGGT AAATACTTTA
4501 TTGAAAGGTT ATGGCGACCA ATTTGCAATT AACTTTTCTT GAGTACTTAG TAAGAATAGA
4561 GTCAGTCGAG GTTTTTTCAT TTCGGGTCGT GGGGATGATA CTGAAAATTT GTTTGTAATC
4621 TCTCAAAATT GCTGTTTCTG TGGCTACGTC TGTCTTTTGG GATATTGTTT CCATCAAGTC
4681 TGTCAACATA CTGTTAAGTT AGATGTTGAT AAAAGAGACT GAATTATAAT ACAAAACAAT
4741 AAATCACTTG GACAATATTT TATTTCACAT GAGACATTAA GGTTGATTTT CCCAATCTGG
4801 TCAGTTATAA CCGAATAAGG ATCTTGAAAA ATCATGGGAT CTTACTTTTA TCAAATGAAG
4861 TTAACGTAAA AGTTGATAAA GAAAATTATT TAATTCTAAG TGCCGTTGGC ATAAATATTT
4921 TGTGTTTTGT TAATGAATGA ATAACCAGGT AAGCTGGATT TTCATTTTTT AATTACTCGT
4981 TACAATATGC TATTTATTTA TATAAAGAGT TTGTGCCCAT TTAACCAGTA AACAAATTTG
5041 TTCAACCGTA ACTTAGCTTC ATCGACTTTT GGCCTCGCCT GGTCAGAATC TAGGGCCGTT
5101 ATCCTATTTA TTTATGATAA ATAAAATTTA ATTATCTTTA ATAAGCTGAA TATGTGGATT
5161 TGTGCTCAAT CTTGGATTCA AGTATGTATT CCTTTTGGTA CCCTGCTTTA TTTTAAGGCA
5221 GATGAAGAGG ATGCCAACAT GACACAATAT CGATTACGAC TGTAACATTA AAGTCAGTTA
5281 TAAATTTTAT GATTAAAATG AAATTTTAGT AGAAAATCGT ATTCTATTCC GCCATTTACA
5341 ATAGCATCCT CTTTAATATC ATTAATCTCA GATAAAACAA ATAATTACAA TGTGAATAGA
5401 ATAATGACTT ACAAAATAAG CACTAAATCT TCAGATGAAC TCTTAACTGA CAACACTATT
5461 TTATAAAATA ATTGAGGTTA TTATGTATAG CACGGCTGTA TTACTCAATA AAATCAGTCC
5521 CACTCGCGAC GGTCAGACGA TGACTCTTGC GGATCTGCAA TATTTATCCT TCAGTGAACT
5581 GAGAAAAATC TTTGATGACC AGCTCAGTTG GGGAGAGGCT CGCCATCTCT ATCATGAAAC
5641 TATAGAGCAG AAAAAAAATA ATCGCTTGCT GGAAGCGCGT ATTTTTACCC GTGCCAACCC
5701 ACAATTATCC GGTGCTATCC GACTCGGTAT TGAACGAGAC AGCGTTTCAC GCAGTTATGA
5761 TGAAATGTTT GGTGCCCGTT CTTCTTCCTT TGTGAAACCG GGTTCAGTGG CTTCCATGTT
5821 TTCACCGGCT GGCTATCTCA CCGAATTGTA TCGTGAAGCG AAGGACTTAC ATTTTTCAAG
5881 CTCTGCTTAT CATCTTGATA ATCGCCGTCC GGATCTGGCT GATCTGACTC TGAGCCAGAG
5941 TAATATGGAT ACAGAAATTT CCACCCTGAC ACTGTCTAAC GAACTGTTGC TGGAGCTATT
6001 ACCCGCAAGA CCGGAGGTGA TTCGGACGCA TTGATGGAGA GCCTGTCAAC TTACCGTCAG
6061 GCCATTGATA CCCCTTACCA TCAGCCTTAC GAGACTATCC GTCAGGTCAT TATGACCCAT
6121 GACAGTACAC TGTCAGCGCT GTCCCGTAAT CCTGAGGTGA TGGGGCAGGC GGAAGGGGCT
6181 TCATTACTGG CGATTCTGGC CAATATTTCT CCAGAACTGT ATAACATTTT GACCGAAGAG
6241 ATTACGGAAA AGAACGCTGA TGCTTTATTT GCGCAAAACT TCAGTGAAAA TATCACGCCC
6301 GAAAATTTCG CGTCACAATC ATGGATAGCC AAGTATTATG GTCTTGAACT TTCTGAGGTG
6361 CAAAAATACC TCGGGATGTT GCAGAATGGC TATTCTGACA GCACCTCTGC TTATGTGGAT
6421 AATATCTCAA CGGGTTTAGT GGTCAATAAT GAAAGTAAAC TCGAAGCTTA CAAAATAACA
6481 CGTGTAAAAA CAGATGATTA TGATAAACAT GTAAATTACT TTGATCTGAT GTATGAAGGA
6541 AATAATCAAT TCTTTATATG TGCTAATTTT AAGATATCGA GAGAATTTGG GGCGACTCTT
6601 AGGAAAAACT CAGGGACAAG TGGCATTGTC GGCAGCCTTT CCGGTCCCCT GGTAGCCAAT
6661 ACTAATTTCA AAAGCAATTA CTTAAGTAAC ATATCTGATA ATGAATACAG AAATGGCGTA
6721 AAAATATATG CCTATCGCTA TACGTCTTCC ACCAGCGCCA CAAATCAGGG CGGCGGAATA
6781 TTCACTTTTG AGTCTTATCC CCTGACTATA TTTGCGCTCA AACTGAATAA AGCCATTCGC
6841 TTGTGCCTGA CTAGCGGGCT TTCACCGAAT GAACTGCAAA CTATCGTACG CAGTGACAAT
6901 GCACAAGGCA TCATCAACGA CTCCGTTCTG ACCAAAGTTT TCTATACTCT GTTCTACAGT
6961 CACCGTTATG CACTGAGCTT TGATGATGCA CAGGTACTGA ACGGATCGGT CATTAATCAA
7021 TATGCCCGAC GATGACAGTG TCAGTCATTT TAACCGTCTC TTTAATACCC CGCCGCTGAA
7081 AGGGAAAATC TTTGAAGCCG ACGGCAACAC GGTCAGCATT GATCCGGATG AAGAACAATC
7141 TACCTTTGCC CGTTCAGCCC TGATGCGTGG TCTGGGGATC AACAGTGGTG AACTGTATCA
7201 GTTAGGCAAA CTGGCGGGTG TATTGGACAC ACAAAATATC CTCACACTTT CTGTCCCTGT
7261 TATATCTTCA CTGTATCGCC TCACGTTACT GGCCCGTGCC CATCAGCTGA CGGTTAATGA
7321 ACTGTGTATG CTTTATGGTT TTTCGCCGTT CAATGGCAAA ACAACGGCTT CTTTGTCTTC

SDOCID: <WO___9808388A1TI_>

Fig.2.

7381	CGGGGAGTTG	TCACGGCTGG	TTATCTGGTT	GTATCAGGTG	ACGCAGTGGC	TGACTGAGGG
7441	CGGAAATCAC	CACTGAAGCG	ATCTGGTTAT	TATGTACGCC	AGAGTTCAGC	GGGAATATTT
7501	CACCGGAAAT	CAGTAATCTG	CTTAATACTC	TCCGACCCCG	TATTAGTGAA	GACATGGCAC
7561	AAAGTAGTGA	CCGGGAGCTT	CAGGCTGAAA	TTCTCGCGCC	GTTTATTGCT	GCAACGCTGC
7621	ATCTGGCGTC	ACCAGATATG	GCGCGGTATA	TCCTGTTGTG	GACTGATAAC	CTGCGGCCGG
7681	GCGGCCTGAA	TATCGCCGGA	TTTATGATGC	TGGTGCTGAA	AGAGACGCTG	AGTGATGAGG
7741	AAACGACCCA	ACTGGTTCAA	TTCTGCCATG	TAATGGCACA	GTTATCGCTT	TCCGTGCAGA
7801	CACTGCGTCT	CAGTGAAGCA	GAGCTTTCTG	TGCTGGTCAT	TTCCGATTTT	GTGGTACTGG
7861	GTGCGAGAAG	CCAACCGCCG	GACAACACAA	TATTGATACT	CTGTTCTCAC	TCTACCGATT
7921	CCACCAGTGG	ATTAATGGGC	TGGGAAATCC	CGGCTCTGAC	ACGCTGGATA	TGCTGCGCCA
7981	AGCAGACACT	CACGGGCGAC	AGACTGGGCC	TCCGTGATGG	GGCTGGACAT	CAGTATGGTA
8041	ACGCAGGCCA	TGGGTTCCCG	CCGGCGTGAA	CCAACTTCAG	TGTTGGCAGG	ATATCAACCC
8101	CGTGTTGCAG	TGGATACATG	TGGCATCAGC	ACTGCTCACT	GATGCCGTCG	GTTATCCGTA
8161	CGCTGGTGAA	TATCCGTTAC	GTGACTGCAT	TAAACAAAGC	CGAGTCGAAT	CTGCCTGCCT
8221	GGCATAAGTG	GCAGACGCTG	GCAGAAAATA	TGGCAGCCGG	ACTGAGTACA	CAACAGGCTC
8281	AGACGCTGGC	GGATTATACC	GCAGAGCGCC	TGAGTAACGT	GTTGTGCAAT	TGGTTTCTGG
8341	CGAATATCCA	GCCAGAAGGG	GTGTCCCTGC	ACAGCCGGGA	TGACCTGTAC	AGCTATTTCC
8401	TGATTGATAA	TCAGGTCTCT	TCTGCCATAA	AAACCACCCG	ACTGGCAGAG	GCCATTGCCG
8461	GTATTCAGCT	CTACATCAAC	CGGGCGCTGA	ACCGGATAGA	GCCTAATGCC	CGTGCCGATG
8521	TGTCAACCCG	CCAGTTTTTT	ACCGACTGGA	CGGTGAATAA	CCGTTACAGC	ACCTGGGGCG
8581	GGGTGTCGCG	GCTGGTTTAT	TATCCGGAAA	ATTACATTGA	CCCGACCCAG	CGTATCGGGC
8641	AGACCCGGAT	GATGGATGAA	CTGCTGGAAG	ATATCAGCCA	GAGTCAGCTC	AGCCGGGACA
8701	CGGTGGAAGA	GGCCTTTAAA	ACTTACCTGA	CCGCTTTGAA	ACCGTGGCAG	ACCTGAAAGT
8761	TGTCAGCGCT	ATCACCGACA	ACGTCAACAG	CAACACCGGA	CTGACCTGGT	TTGTCGGCCA
8821	AACGCGGGAG	AACCTGCCGG	AATATTACTG	GCGTAACGTG	CATATATCAC	GGATGCAGGC
8881	GGGTGAACTG	GCCGCCGATG	CCTGGAAAGA	TTGGACGAAG	ATTGATACAG	CGGTCAACCC
8941	ATACAAGGAT	GCAATACGTC	CGGTCATATT	CAGGGAACGT	TTGCACCTTA	TCGTGGGTAG
9001	AAAAAGAGGA	AGTGGCGAAA	AATGGTACTG	ATCCGGTGGA	AACCTATGAC	CGTTTTACTC
9061	TGAAACTGGC	GTTTCTGCGT	CATGATGGCA	GTTGGAGTGC	CCCCTGGTCT	TACGATATCA
9121	CAACGCAGGT	GGAGGCGGTC	ACTGACAAAA	AACCTGACAC	TGAACGGCTG	GCGCTGGCCG
9181	CATCAGGCTT	TCAGGGCGAG	GATACTCTGC	TGGTGTTTGT	GTACAAAACC	GGGGTGAGTT
9241	ACCCGGATTT	TGGCGACAAC	AATAAAAATG	TGGCAGGCAT	GACCATTTAC	GGCGATGGCT
9301	CCTTCAAAAA	GATGGAGAAC	ACAGCACTCA	GCGTTACAGC	CAACTGAAAA	ATACCTTTGA
9361	TATCATTCAT	ACTCAAGGCA	ACGACTTGGT	AAGAAAGGCC	AGCTATCGTT	TCGCGCAGGA
9421	TTTTGAAGTG	CCTGCCTCGT	TGAATATGGG	TTCTGCCATC	GGTGATGATA	GTCTGACGGT
9481	GATGGAAAAC	GGGAATATTC	CGCAGATAAC	CAGTAAATAC	TCCAGCGATA	ACCTTGCTAT
9541	TACGCTACAT	AACGCCGCTT	TCACTGTCAG	ATATGATGGC	AGTGGCAATG	TCATCAGAAA
9601	CAAACAAATC	AGCGCCATGA	AACTGACGGG	GTTGGATGAA	AGTCCCAGTA	CGGCAATGCA
9661	TTTATCATCG	CAAATACCGT	TAAACATTAT	GGCGGTTACT	CTGATCTGGG	GGGCCCGATC
9721	ACCGTTTTTA	TTAAAACGGA	AAAACTATAT	TGCATCAGTT	CAAGGCCACT	TGATGAACGC
9781	AGATTACACT	AGGCGTTTGA	TTCTAACACC	AGTTGAAAAT	AATTATTATG	CCAGATTGTT
9841	CGAGTTTCCA	TTTTCTCCAA	ACACAATTTT	AAACACCGTT	TTCACGGTTG	GTAGCAATAA
9901	AACCAGTGAT	TTTAAAAAGT	GCAGTTATGC	TGTTGATGGT	AATAATTCTC	AGGGCTTCCA
9961	GATATTTAGT	TCCTATCAAT	CATCCGGCTG	GCTGGATATT	GACACAGGTA	TTAACAATAC
10021	TGATGTCAAA	ATTACGGTGG	TAGCTGGCAG	TAAAACCCAC	ACCTTTACGG	CCAGTGACCA
10081	TATTGCTTCC	TTGCCGGCAA	ACAGTTTTGA	TGCTATGCCG	TACACCTTTA	AGCCACTGGA
10141	AATCGATGCT	TCATCGTTGG	CCTTTACCAA	TAATATTGCT	CCTCTGGATA	TCGTTTTTGA
10201	GACCAAAGCC	AAAGACGGGC	GAGTGCTGGG	TAAGATCAAG	CAAACATTAT	CGGTGAAACG
10261	GGTAAATTAT	AATCCGGAAG	ATATTCTGTT	TCTGCGTGAA	ACTCATTCGG	GTGCCCAATA
10321	TATGCAGCTC	GGGGTGTATC	GTATTCGTCT	TAATACCCTG	CTGGCTTCTC	AACTGGTATC
10381	CAGAGCAAAC	ACGGGCATTG	ATACTATCCT	GACAATGGAA	ACCCAGCGGT	TACCGGAACC
10441	TCCGTTGGGA	GAAGGCTTCT	TTGCCAACTT	TGTTCTGCCT	AAATATGACC	CTGCTGAACA
10501	TGGCGATGAG	CGGTGGTTTA	AAATCCATAT	CGGGAATGTT	GGCGGTAACA	CGGGAAGGCA
10561	GCCTTATTAC	AGCGGAATGT	TATCCGATAC	GTCGGAAACC	AGTATGACAC	TGTTTGTCCC
10621	TTATGCCGAA	GGGTATTACA	TGCATGAAGG	TGTCAGATTG	GGGGTTGGAT	ACCAGAAAAT
10681	TACCTATGAC	AACACTTGGG	AATCTGCTTT	CTTTTATTTT	GATGAGACAA	AACAGCAATT
10741	TGTATTAATT	AACGATGCTG	ATCATGATTC	AGGAATGACG	CAACAGGGGA	TCGTGAAAAA
10801	TATCAAGAAA	TACAAAGGAT	TTTTGAATGT	TTCTATCGCA	ACGGGCTATT	CCGCCCCGAT
10861	GGATTTCAAT	AGTGCCAGCG	CCCTCTATTA	CTGGGAATGT	TCTATTACAC	CCCGATGATG
10921	TGCTTCCAGC	GTTTGCTACA	GGAAAAACAA	TTCGACGAAG	CCACACAATG	GATAAACTAC
10981	GTCTATAATC	CCGCCGGCTA	TATCGTTAAC	GGAGAAATCG	CCCCCTGGAT	CTGGAACTGC
11041	CGGCCGCTGG	AAGAGACACT	CCTGGAATGC	CAATCCGTTG	GATGCCATTG	ATCCGGATGC
11101	CGTCGCACAA	TATGACCCGA	CACACTATAA	AGTTGCCACC	TTTATGCGCC	TGTTGGATCA
11161	ACTTATTCTG	CGCGGCGATA	TGGCCTATCG	CGAACTGACC	CGCGATGCGT	TGAATGAAGC

BNSDOCID: <WO___9808388A1TI_>

Fig.2.

11221 CAAGATGTGG TATGTGCGTG CTTTGGAATT GCTGGGTGAT GAGCCGGAGG ATTACGGCAG
11281 CCAACAGTGG GCCGCACCGT CTCTTTCCGT GGCGGGCAAC CACACTGTGC AAGCGGGCTA
11341 TCAACAAGAC CTTACGGCGC TAGACAACGG AGAAGGTTGC ACTCAACCCC GCAACGCTAA
11401 CTCGTTGGTG GTTTGGTCCT GCCGGAATAT AACCCGGAAT CAACCGATTA CTGGCAAACC
11461 TGCGTTTGCG CCTGGTTAAC CTGCGCCATA ATCCTTCCAT GACGGGCAAC CGTTATCGCT
11521 GGCGAATTAC GCGAGCCTAC GATCCGAAAG CGCTGCTCAC CAGTATGGTA CAGCCTTCTC
11581 AGGGCGGTAG TGCAGTGCTG CCCGGCACAT TGTCGTTATA CCGCTTCCCG GTGATGCTGG
11641 AGCGGGCCCG CAATCTGGTA GCGCAATTAA CCCAGTTCGG CACCTCTCTG CTCAGTATGG
11701 CAGAGCATGA TGATGCCGAT GAACTCACCA CGTTGCTACT ACAGCAGGGT ATGGAACTGG
12761 CGACACAGAG CATCCGTATT CAGCAACGAA CTGTCGATGA AGTGGATGCT GATATTGCTG
11821 TATTGGCAGA GAGCCGCCGC AGTGCACAAA ATCGTCTGGA AAAATACCAG CAGCTGTATG
11881 ACGAGGATAT CAACCACGGA GAACAGCGTG CGATGTCACT GTTTGATGCG GCGGCAGGTC
11941 AGTCTCTGGC CGGGCAGGCG CTCTCAGTAG CAGAAGGGGT GGCTGACTTA GTTCCAAACG
12001 TGTTCGGTTT CGCTTGTGGC GGCAGTCGTT GGGGGCAGC ACTGCGTGCT TCCGCCTCCG
12061 TGATGTCGCT TTCTGCCACA GCTTCCCAAT ATTCCGCAGA CAAAATCAGC CGTTCGGAAG
12121 CCTACCGCCG CCGCCGTCAG GAGTGGAAA TTCAGCGTGA TAATGCTGAC GGTGAAGTCA
12181 AACAAATGGA TGCCCAGCTG GAAAGCCTGA AAATACGCGG CGAAGCAGCA CAGATGCAGG
12241 TGGAATATCA GGAGACCCAG CAGGCCCATA CTCAGGCTCA GTTAGAGCTG TTACAGCGTA
12301 AATTCACAAA CAAAGCGCTT TACAGTTGGA TGCGCGGCAA GCTGAGTGCT ATCTATTACC
12361 AGTTCTTTGA CCTGACCCAG TCCTTCTGCC TGATGGCACA GGAAGCGCTG CGCCGCGAGC
12421 TGACCGACAA CGGTGTTACC TTTATCCGGG GTGGGGCCTG GAACGGTACG ACTGCGGGTT
12481 TGATGGCGGG TGAAACGTTG CTGCTGAATC TGGCAGAAAT GGAAAAAGTC TGGCTGGAGC
12541 GTGATGAGCG GGCACTGGAA GTGACCCGTA CCGTCTCGTT GGCACAGTTC TATCAGGCCT
12601 TATCATCAGA CAACTTTAAT CTGACCGAAA AACTCACGCA ATTCCTGCGT GAAGGGAAAG
12661 GCAACGTAGG AGCTTCCGGC AATGAATTAA AACTCAGTAA CCGCCAGATA GAAGCCTCAG
12721 TGCGATTGTC TGATTTGAAA ATTTTCAGCG ATACCCCGGA AAGCTTTGGC AATACCCGTC
12781 AGTTGAAACA AGTGAGTGTC ACCTTGCCGG CGCTGGTTGG TCCGTATGAA GATATCCGGG
12841 CGGTGCTGAA TTACGGCGGC AGCATCGTCA TGCCACGCGG TTGCAGTGCT ATTGCTCTCT
12901 CCCACGGCGT GAATGACAGT GGTCAATTTA TGCTGGATTT CAACGATTCC CGTTATCTGC
12961 CGTTTGAAGG TATTTCCGTG AATGACAGCG GTAGCCTGAC GTTGAGTTTC CCGGATGCGA
13021 CTGATCGACA GAAAGCGCTG CTGGAGAGCC TGAGCGATAT CATTCTGCAT ATCCGCTATA
13081 CCATTCGTTC TTAATTAAAA CATTGTGATA GGCAGGCTCC TGAGGGAGCC TGTTTAAGGA
13141 GTTTTTATGC AGGGTTCAAC ACCTTTGAAA CTTGAAATAC CGTCATTGCC CTCTGGGGGC
13201 GGATCACTAA AAGGAATGGG AGAAGCACTC AATGCCGTCG GAGCGGAAGG GGAGCGTCAT
13261 TTTCACTGCC CTTGCCGATC TCTGTCCGGC GTGGTCTGGT GCCGGTGCTA TCACTGAATT
13321 ACAGCAGTAC TGCTGGCAAT GGGTCATTCG GGATGGGGTG GCAATGTGGG GTTGGTTTTA
13381 TCAGCCTGCG TACCGCCAAG GGCGTTCCGC ACTATACGGG ACAAGATGAG TATCTCGGGC
13461 CGGATGGGGA AGTGTTGAGT ATTGTGCCGG ACAGCCAAGG GCAACCAGAG CAACGCACCG
13501 CAACCTCACT GTTGGGGACG GTTCTGACAC AGCCGCCTAC TGTTACCCGC TATCAGTCCC
13561 GCGTGGCAGA AAAAATCGTT CGTTTAGAAC ACTGGCAGCC ACAGCAGAGA CGTGAGGAAG
13621 AGACGTCTTT TTGGGTACTT TTTACTGCGG ATGGTTTAGT GCACCTATTC GGTAAGCATC
13681 ATCATGCACG TATTGCTGAC CCGCAGGATG AAACCAGAAT TGCCCGCTGG CTGATGGAGG
13741 AAACCGTCAC GCATACCGGG GAACATATTT ACTATCACTA TCGGGCAGAA GACGATCTTG
13801 ACTGTGATGA GCATGAACTT GCTCAGCATT CAGGTGTTAC GGCCCACCGT TATCCTGGCA
13861 AGTCCACTAT GGCAATACTC AGCCGGAAAC CGCTTTTTTC GCGGTAAAAT CAGGTATCCC
13921 TGTTGATAAT GACTGGTTGT TTCATCTGGT ATTTGATTAC GGTGAGCGCT TATCTTCGCT
13981 GAACTCCGTA CCCGAATTCA ATGTGTCAGA AAACAATGTG TCTGAAAACA ATGTGTCTGA
14041 AAAATGGCGT TGTCGTCCGG ACAGTTTCTC CCGCTATGAA TATGGGTTTG AAATTCGAAC
14101 CCGTCGCTTG TGTCGCCAAG TTCTGATGTT TCATCAGCTG AAAGCGCTGG CAGGGGAAAA
14161 GGTTGCAGAA GAAACACCGG CGCTGGTTTC CCGTCTTATT CTGGATTATG ACCTGAACAA
14221 CAAGGTTTCC TTGCTGCAAA CGGCCCGCAG ACTGGCCCAT GAAACGGACG GTACGCCAGT
14281 GATGATGTCC CCGCTGGAAA TGGATTATCA ACGTGTTAAT CATGGCGTGA ATCTGAACTG
14341 GCAGTCCATG CCGCAGTTAG AAAAAATGAA CACGTTGCAG CCATACCAAT TGGTTGATTT
14401 ATATGGAGAA GGAATTTCCG GCGTTACTTT ATCAGGATAC TCAGAAAGCC TGGTGGTACC
14461 GTGCTCCGGT ACGGGATATC ACTGCCGAAG GAACGAATGC GGTTACCTAT GAGGAGGCGA
14521 AACCACTGCC ACATATTCCG GCACAACAGG AAAGCGCGAT GTTGTTGGAC ATCAATGGTG
14581 ACGGGCGTCT GGATTGGGTG ATTACGGCAT CAGGGTTACG GGGCTACCAC ACCATGTCAC
14641 CGGAAGGTGA ATGGACACCC TTTATTCCAT TATCCGCTGT GCCAATGGAA TATTTCCATC
14701 CGCAGGCAAA ACTGGCTGAT ATTGATGGGG CTGGGCTGCC TGACTTAGCG CTTATCGGGC
14761 CAAATAGTGT ACGTGTCTGG TCAAATAATC CGGCAGGATG GGATCGCGCT CAGGATGTTA
14821 TTCATTTGTC AAATAAGCCA CTGCCGGTTC CCGGCAAAAA TAAGCGTCAT CTTGTCGCAT
14881 TCAGTGATAT GACAGGCTCC GGGCAATCAC ATCTGGTGGA AGTTACGGCA AATAGCGTGC
14941 GCTACTGGCC GAACCTGGGG CATGGAAAAT TTGGTGAGCC TCTGATGATA ACAGGCTTCC
15001 AAATTACGGG GAAACGTTTA ACCCCCACAG ACTGTATATG GTAGACCTAA ATGGCTCAGG

SDOCID: <WO___9808388A1TI_>

Fig.2.

15061	CACCACCCGA	TTTTATTTAT	GCCCGCAATA	CTTACCTTGA	ACTCTATGCC	AATGAAAGCG
15121	GCAATCATTC	TGCTGAACCT	CAGCGTATTG	ATCTGCCGGA	TGGGGTACGT	TTTGATGATA
15181	CTTGTCGGTT	ACAAATAGCG	GATACACAAG	GATTAGGGAC	TGCCAGCATT	ATTTTGACGA
15241	TCCCCCATAT	GAAGGTGCAG	CACTGGCGAT	TGGATATGAC	CATATTCAAG	CCTTGGCTGC
15301	TGAATGCCGT	CAATAACAAT	ATGGGAACAG	AAACCACGCT	GTATTATCGC	AGCTCTGCCC
15361	AGTTCTGGCT	GGATGAGAAA	TTACAGGCTT	CTGAATCCGG	GATGACGGTG	GTCAGCTACT
15421	TACCGTTCCC	GGTGCATGTG	TTGTGGCGCA	CGGAAGTGCT	GGATGAAATT	TCCGGTAACC
15481	GATTGACCAG	CCATTATCAT	TACTCACATG	GTGCCTGGGA	TGGTCTGGAA	CGGGAGTTTC
15541	GTGGTTTTGG	GCGGGTGACG	CAAACTGATA	TTGATTCACG	GGCGAGTGCG	ACACAGGGGA
15601	CACATGCTGA	ACCACCGGCA	CCTTCGCGCA	CGGTTAATTG	GTACGGCACT	GGCGTACGGG
15661	AAGTCGATAT	TCTTCTGCCC	ACGGAATATT	GGCAGGGGGA	TCAACAGGCA	TTTCCCCATT
15721	TTACCCCACG	CTTTACCCGT	TATGACGAAA	AATCCGGTGG	TGATATGACG	GTCACGCCGA
15781	GCGAACAGGA	AGAATACTGG	TTACATCGAG	CCTTAAAAGG	ACAACGTTTA	CGCAGTGAGC
15841	TGTATGGGGA	TGATGATTCT	ATACTGGCCG	GTACGCCTTA	TTCAGTGGAT	GAATCCCGCA
15901	CCCAAGTACG	TTTGTTACCG	GTGATGGTAT	CGGACGTGCC	TGCGGTACTG	GTTTCGGTGG
15961	CCGAATCCCG	CCAATACCGA	TATGAAGGGG	TTGTTACCGA	TTCCACAGTG	CAGCCAAAAG
16021	ATTGTCCTTA	AATATGATGC	GTTAGGATTT	CCCCAGGACA	ATCTTGAGAT	TGCCTATTCG
16081	AGACGTCCAC	AGCCTGAGTT	CTCGCCTTAT	CCGGATACCC	TGCCCGAAAC	ACTTTTCACC
16141	AGCAGTTTCG	ACGAACAGCA	GATGTTCCTT	CGTCTGACAC	GCCAGCGTTT	TTCTTATCAC
16201	CATCTGAATC	ATGATGATAA	TACGTGGATC	ACAGGGCTTA	TGGATACCTC	ACGCAGTGAC
16261	GCACGTATTT	ATCAAGCCGA	TAAAGTGCCG	GACGGTGGAT	TTTCCCTTGA	ATGGTTTTCT
16321	GCCACAGGTG	CAGGAGCATT	GTTGTTGCCT	GATGCCGCAG	CCGATTATCT	GGGACATCAG
16381	CGTGTAGCAT	ATACCGGTCC	AGAAGAGCAA	CCCGCTATTC	CTCCGCTGGT	GGCATACATT
16441	GAAACCGCAG	AGTTTGATGA	ACGATCGTTG	GCCGCTTTTG	AGGAGGTGAT	GGATGAGCAG
16501	GAGCTGACAA	AACAGCTGAA	TGATGCGGGC	TGGAATACGG	CAAAAGTGCC	GTTCAGTGAA
16561	AAGACAGATT	TCCATGTCTG	GGTGGACAAA	AAGGAATTTA	CAGAATATGC	CGGTGCAGAC
16621	GGATTCTATC	GGCCATTGGT	GCAACGGGAA	ACCAAGCTTA	CAGGTCAAAC	GACAGTGACG
16681	TGGGATAGCC	ATTACTGTGT	TATCACCGCA	ACAGAGGATG	CGGCTGGCCT	GCGTATGCAA
16741	GCGCATTACG	ATTATCGATT	TATGGTTGCC	CATAACACCA	CAGATATCAA	TGATAACTAT
16801	CACACCGTGA	CGTTTGATGC	ACTGGGGACG	GTAACCAGCT	TCCGTTTCTG	GGGGACTGAA
16861	AACGGTGAAA	AACAAGGATA	TACCCCTGCG	GAAAATGAAA	CTGTCCCCTT	TATTGTCCCC
16921	ACAACGGTGG	ATGATGCTCT	GGCATTGAAA	CCCGGCATAC	CTGTTGCAGG	GCTGATGGTT
16981	TATGCCCCTC	TGAGCTGGAT	GGTTCAGGCC	AGTTTTTCTA	ATGATGGGGA	GCTTTATGGA
17041	GAGCTGAAAC	CGGCTGGGAT	CATCACTGAA	GATGGTTATC	TCCTGTCGCT	TGCTTTTCGC
17101	CGCTGGCATC	AAAATAACCC	TGCCGCTGCC	ATGCCAAAGC	AAGTCAATTC	ACAGAACCCA
17161	CCCCATGTAC	TGAGTGTGAT	CACCGACCGC	TATGATGCCG	ATCCGGAACA	ACAATTACGT
17221	CAAACGTTTA	CGTTTAGTGA	TGGTTTTGGG	CGAAACCTTA	CAAACAGCCG	TACGCCATGA
17281	AAGTGGTGAA	GCCTGGGTAC	CTGATGAGTA	TGGAGCCAAT	GTGGCTGAAA	ATCAAGGCGC
17341	CCCTGAAACG	GGCGATTACA	AATTTCCCGT	TGGGCAATTT	CCCGGACGTA	CAGAATATTA
17401	ACGGGAAAAG	GCAAAGCCCC	TGCGTTACGT	TTCAAACCGT	ATTCCTGAAA	TAATTTGGGC
17461	AACTATGTCA	AGTTGACCAA	AAAATGCCCG	GCAGGATATG	TATGCCGATA	CCCATTACTA
17521	TGATCCGTTG	GGGCGTGAAT	ATCAGGTTAT	CACGCCAAAG	GCGGGTTGCG	TCGATCCTTA
17581	TTCACTCCCT	GGTTTGTGGT	GAATGAAGTT	GAAAATGACA	CTCCCGGTGA	ATGACAGCAT
17641	AAAGCTCAGT	GATGCCTGTT	CACTGAACAG	ACATCACTCC	ATTTAGGAAT	GAATCATGAA
17701	GAATTTCGTT	CACAGCAATA	CGCCATCCGT	CACCGTACTG	GACAACCGTG	GTCAGACAGT
17761	ACGCGAAATA	GCCTGGTATC	GGCACCCCGA	TACACCTCAG	GTAACCGATG	AACGCATCAC
17821	CGGTTATCAA	TATGATGCTC	AAGGATCTCT	GACTCAGAGT	ATTGATCCGC	GATTTTATGA
17881	ACGCCAGCAG	ACAGCGAGTG	ACAAGAACGC	CATTACACCC	AATCTTATTC	TCTTGTCATC
17941	ACTCAGTAAG	AAGGCATTGC	GTACGCAAAG	TCTGGATGCC	GGAACCCGTG	TCGCCCTGCA
18001	TGATGTTGCC	GGGCGTCCCG	TTTTAGCTCT	CAGCGCCAAT	GGCGTTAGCC	GAACGTTTCA
18061	GTATGAAAGT	GATAACCTTC	CGGGACGATT	GCTAACGATT	ACCGAGCAGG	TAAAAGGAGA
18121	GAACGCCTGT	ATCACGGAGC	GATTGATTTG	GTCAGGAAAT	ACGCCGGCAG	AAAAAGGCAA
18181	TAATTTGGCC	GGCCAGTGCG	TGGTCCATTA	TGATCCCACC	GGAATGAATC	AAACCAACAG
18241	CATATTGTTA	ACCAGCATAC	CCTTGTCCAT	CACACAGCAA	TTAGTGAAAG	ATGACAGCGA
18301	AGCCGATTGG	CACGGTATGG	ATGAATTTGG	CTGGAAAAAC	GCGCTGGCGC	CGGAAAGCTT
18361	CACTTCTGTC	AGCACAACGG	ATGCTACCGG	CACGGTATTA	ACGAGTACAG	ATGCTGCCGG
18421	AAACAAGCAA	CGTATCGCCT	ATGATGTGGC	CGGTCTGCTT	CAAGGCAGTT	GGTTGGCGCT
18481	GAAGGGGAAA	CAAGAACAAG	TTATCGTGAA	ATCCCTGACC	TATTCGGCTG	CCAGCCAGAA
18541	GCTACGGGAG	GAACATGGTA	ACGGGATAGT	GACTACATAT	ACCTATGAAC	CCGAGACGCA
18601	ACGAGTTATT	GGCATAAAAA	CAGAACGTCC	TTCCGGTCAT	GCCGCTGGGG	AGAAAATTTT
18661	ACAAAACCTG	CGTTATGAAT	ATGATCCTGT	CGGAAATGTG	CTGAAATCAA	CTAATGATGC
18721	TGAAATTACC	CGCTTTTGGC	GCAACCAGAA	AATTGTACCG	GAAAATACTT	ACACCTATGA
18781	CAGCCTGTAC	CAGCTGGTTT	CCGTCACTGG	GCGTGAAATG	GCGAATATTG	GCCGACAAAA
18841	AAACCAGTTA	CCCATCCCCG	CTCTGATTGA	TAACAATACT	TATACGAATT	ACTCTCGCAC

BNSDOCID: <WO___9808388A1TI_>

Fig.2.

18901	TTACGACTAT	GATCGTGGGG	GAATCTGACC	AGAATCGCAT	AATTCACGAT	CACCGGTAAT
18961	AACTATACAA	CGAACATGAC	CGTTTCAGAT	CACAGCAACC	GGGCTGTACT	GGAAGAGCTG
19021	GCGCAAGATC	CCACTCAGGT	GGATATGTTG	TTCACCCCCG	GCGGGCATCA	GACCCGGCTT
19081	GTTCCCGGTC	AGGATCTTTT	CTGGACACCC	CGTGACGAAT	TGCAACAAGT	GATATTGGTC
19141	AATAGGGAAA	ATACGACGCC	TGATCAGGAA	TTCTACCGTT	ATGATGCAGA	CAGTCAGCGT
19201	GTCATTAAGA	CTCATATTCA	GAAGACAGGT	AACAGTGAGC	AAATACAGCG	AACATTATAT
19261	TTGCCAGAGC	TGGAATGGCG	CACGACATAT	AGCGGCAATA	CATTAAAAGA	GTTTTTGCAG
19321	GTCATCACTG	TCGGTGAAGC	GGGTCAGGCA	CAAGTGCGGG	TGCTGCATTG	GGAAACAGGC
19381	AAACCGGCGG	ATATCAGCAA	TGATCAGCTG	CGCTACAGTT	ATGGCAACCT	GATTGGCAGT
19441	AGCGGGCTGG	AATTGGGACA	GTGACGGGCA	GATCATTAGT	CAGGAAGAAT	ATTACCCCTA
19501	TGGGGGAACC	GCCGTGTGGG	CACCCGAAAT	CAGTCAGAAG	CTGATTACAC	AAGCCGGCGT
19561	TATTCTGGCA	AAGAGCGGGA	TGCAACAGGG	TTGTATTACT	ACGGCTATCG	TTATTATCAA
19621	TCGTGGACAG	GGCGATGGTT	GAGTGTAGAT	CCTGCCGGTG	AGGCCGATGG	TCTCAATTTG
19681	TTCCGAATGT	GCAGGAATAA	CCCCATCGTT	TTTTCTGATT	CTGATGGTCG	TTTCCCCGGT
19741	CAGGGTGTCC	TTGCCTGGAT	AGGGAAAAAA	GCGTATCGAA	AGGCAGTCAA	CATCACGACA
19801	GAACACCTGC	TTGAACAAGG	CGCTTCCTTT	GATACGTTCT	TGAAATTAAA	CCGAGGATTG
19861	CGAACGTTTG	TTTTGGGTGT	GGGGGTACAA	GTCTGGGGGT	GAAGCGGCCA	CGATTGCAGG
19921	AGCGTCGCCT	TGGGGGATCG	TCGGGGCTGC	CATTGGTGGT	TTTGTCTCCG	GGGCGGTGAT
19981	GGGGTTTTTC	GCGAACAACA	TCTCAGAAAA	AATTGGGGAA	GTTTTAAGTT	ATCTGACGCG
20041	TAAACGTTCT	GCTCCTGTTC	AGGTAGGCGC	TTTTGTTGTC	ACATCGCTTG	TGACGTCTGC
20101	ACTATTTAAC	AGCTCTTCGA	CAGGTACCGC	CATTTCCGCA	GCAACAGCGG	TCACCGTTGG
20161	AGGATTAATG	GCTTTAGCCG	GAGAACATAA	CACGGGCATG	GCTATCAGTA	TTGCCACACC
20221	CGCCGGACAA	AGTACGCTGG	ATACGCTCAG	GCCCGGTAAT	GTCAGCGCGC	CAGAGCGGTT
20281	AGGGCACTAT	CAGGCGCAAT	TATTGGCGGC	ATATTACTTG	GCCGCCATCA	GGGAAGTTCT
20341	GAGCTGGGTG	AACGGGCAGC	GATTGGTCCT	ATGTATCCTC	CTCGATGGGG	AAGGATCATT
20401	GGTAATCTAT	GGGATGGCCC	TTATCGGTTT	ATCGGCAGGT	TACTGCTCAG	AAGAGGCATT
20461	AGCTCTGCCA	TTTCCCACGC	TGTCAGTTCC	AGGAGCTGGT	TTGGCCGAAT	GATAGGAGAA
20521	AGTGTCGGGA	GAAATATTTC	TGAAGTATTA	TTACCTTATA	CCCGTACACC	CGGTGAATGG
20581	GTTGGTGCAG	CCATTGGCGG	GACAGCCGCG	GCCGCTCATC	ATGCCGTTGG	AGGGGAAGTT
20641	GCCAATGCCG	CTAGCCGGGT	TACCTGGAGC	GGCTTTAAGC	GGGCTTTTAA	TAACTTCTTC
20701	TTTAACGCCT	CTGCACGTCA	TAATGAATCC	GAAGCATAAC	AATCATGTTC	ATTCCCACTT
20761	TGTCATGGAT	GACAAGGTGG	GTTTTTCGGA	TGTGTGGACA	GAGACCCGTA	CAGGGTCTCT
20821	GTCCAGTTAA	TTTTTGGATC	AAGAACGAAT	GGTGTAACGG	ATATGCAAAA	TGATATCGCT
20881	CAGGCTGAGC	AATAAGCTTT	TCTGTTTACC	ACTCATACCG	GGAAAACTGA	GGGTTAATGT
20941	GCCTGTATCG	GCCACAGGAA	GCCCTTCAAA	TGGCAGGTAC	TTAGCATCAT	TGAAATCCAT
21001	CTGGAATTGA	CCACTGTCAT	TCATGCCATC	TGAGATCACA	ATCGCTTTGC	AGCCACGTGG
21061	CATCATTGTA	CTGCCGCCAT	AACTCAGTAT	TGCCCGGACA	TCCTGATAAG	GCCCTAAAAG
21121	GGCAGGTAAC	GTCACACTGA	TTTGTTTGAT	ACGGCGTGTA	TTACCTAAAC	CGTCAGGATA
21181	ATCGGTAGCA	ATATTCAGAT	CCGATAATTT	GAGGCTGGCT	TGCAGTTGTG	TCCCTTCGAC
21241	GTTCAAACCG	TTAAGCGTTG	TGCCTGCACT	GCCTTCACCT	GCATTGACTA	ACTCAGTCAC
21301	TTTATCTTTT	AAAATGAAAC	TATTTTCTGT	CAGACCAGCA	TACACTTCAG	CCAGAGAAAC
21361	GGTTCTGGTG	ACCTCCAGTG	CCCGTTCATC	TTTTTCCAAA	TAGCTTTTTT	CCATCTGTGC
21421	TAAATTCAGC	ATCAGGGTTT	CACCCGCTAA	TAAACCCGCA	TAAGTCCCAT	GCCAAGCACC
21481	TGGTTTAATA	AAGTGTGCTG	CCGCATTATT	CAATTCATAC	TGATAAGTTT	GCTCTGCCAT
21541	TAAACAGAGT	GAGACCGCCA	AATCATAAAA	CTGATAATAA	ATAGCGGACA	ACGTTCCACG
21601	GAGCCAGTTG	TATAGCGCTG	CATTACTGAA	TTTACTTTGC	AGAAAGGCTA	ACTGCGCCTG
21661	AGTTTGTGCC	TGCTGAGTTT	CCAGATAGTT	TTTTTGTAAT	ACTGCCGCTT	CACGACGTAC
21721	AGCCAGCGTC	GCTAATTGAG	CATCAATTTG	TTTTATCTCA	GCTTCCGCAT	TATTGCGCTG
21781	AATTTCCCAC	TCTTGCCGAC	GGCGACGGTA	TATTTCTGAT	TGGCTGATTT	TGTCTGCGGC
21841	AATACGTGTT	GCTGACGCAG	AAATTTCGAT	ACCAATCGCA	CTGGCATTGA	AAAGCGCCCC
21901	AAAACGGGAA	CCTCCCACAG	CAAAACCGTA	AATATTGGGG	ACGAGATCTG	CCGCGGCGGC
21961	GGCCATATGC	AGGGCTGTGC	CGCTGGTGCT	CAAGACCGAT	GAAGAGAGGT	AAAGATCCAT
22021	CGCTTGTTTT	TCACCAGCGT	TAACATCTTC	GTCGTACAGC	GTATTGAAAC	TGTCAAAACG
22081	AGACTGTGCA	CCATGACGGC	TTTCTTGAAG	CGCCAATTTA	TCAGCATCAA	TTTCAGCCAT
22141	GACCTTATCC	TGCATTTTAA	TACTTTGCAG	GGCTAACTCA	CTGCCTTGAG	TTTGCAGTAT
22201	TTCAGCCAAG	GCTTCTGCAT	CCTGCCGTTC	AGTAATGCTG	AGCAGGGTAT	TGCCAAATTG
22261	TATCAACTGG	CTTACCCCCC	ACTTGGCATT	TTCCAGAATC	ACCGGAAAAC	GGTACATCGG
22321	CATCACTGCA	TGAGGTAAAT	CGCCGCCGCC	TTGTGAAGCA	GTGATGGCAG	CACTGAGTAA
22381	CATGGACGGA	TCTGCGGGCG	TGGCATAGAG	AGATAATGAC	AGTGGCTGAC	CGTCGATTGT
22441	CAGGTTATGG	CGTAAGTTAT	AGAGGCGTTG	CGTCAATGTC	TGCCAGTAAC	CTTGCAGTTT
22501	TTTATTAATT	TGAGGGAGGA	ACAATGCGGT	TAACGAAATT	TGCCGTACGT	TTCGTGGGTA
22561	ATGCAGCGCG	CTGACGCAGT	TGCAGCATTT	TATGTTGATA	ATGATGCCGC	ATTGTTTGGC
22621	TGGCAGCTTC	TTCCAGCCGT	GGCTCTGACC	AATCGTTATC	CAATGAAAAA	TAAGGCTCAT
22681	CACCCAATAA	AGTGAGCGCC	TGTACATACC	ACATTTTAGC	TTCGTTTAAG	GTATCACGTT

Fig.2.

22741 CAAGCTGGCG ATAGGCGCTA TCTCCGCGGG TAATCAACAA ATCCAGCATT TTCATAAAGG
22801 TAGCCACTTT ATAGTGCATC GGATCATGCT GGGCAACGGC GTCCGGATCG ACCGAATCCA
22861 GCGGATTGGC ATTCCAGGAC GTATCTTCCT CCAATGGCCG GACGTTCCAG TAATAATCCT
22921 GCATTTCACC CTGAACCGAA TATCCGGTCG GGTTCAGATA TAGCGCAGCC AGCGTGTCGA
22981 TCCGGTAAAA TCTGCTCTTG CAATAAGCGC TGGAATACCA TCATGGGCGT TGTAATAGAA
23041 CAATCCCAAG AAATAGATTG CATTGGCGCC GTTTGAAATC CATGGGTTCA GTGTTATTTT
23101 TCATGACACG ACTTGAATAC CCCTTTTATA TTTTTTGATA TTTTTTACTA TCCCCTGTTG
23161 TGTCATTCCC GAATCATGAT CGGCATCATT AGTGAATATA AATTGATTTT TCGTCTCATC
23221 AAAATAAAAG AAAGCAGATT CCCAGGATTT GTCATAGATA ATTTTTTTGT ACCCAACCCC
23281 TAATCTGACA CCTTCACGTA TGTAATATCC TTTAGCATAG GGAACAAAGA GCGTTACTGT
23341 GGTTTCAATA TCAGATAACA TTCCTTCGTA ATAAGGTTGT CTGGCAGAAT TGCCATCAAT
23401 ATTCCCAATA TGGATCTTAA ACCAACGTTC ATCACCATGC TCCTCTTTAT TGTAGGGGGG
23461 CAACTTAAAT GTCGCATAAA ACCCTTCACC TAATTGCGGC TCTGGTAAAT TTTGCGTTTC
23521 CATACTTAAA ACATTATCAA TACCAATATT GGCTCTTTCA GCTAATTTTC TGGAAAATAA
23581 AGTATTTAAC CGGGTTCTGT AAGGGCCAAT CTGCATATAT TGTGTGCCTG ATGGCATTTT
23641 ATGCAGTGAT ATAACGTTAC TTGTATCTTT GGATTTTAGT TTTATATGAA TTGGCGATTC
23701 AATAACAATA TCGTTATAAC CGCCGTCGGG TTGCTTAATA ATAAACTCGC TCACCAGAGG
23761 AATATCATAG CCTTCAATAT CAACTTTTAC TTGATTAAAA TCATATACCA TAGGGTCAGA
23821 TTCGTGTGAA GGTTTAGATG CCACATGGTC TTCAGCATTT AACTCCACTA GAATATCAGA
23881 GCCATTTTTT AATAAAAAAC TAATGTTTTT ATCTTGGATC TGTTCGATCA TAGATGAAGC
23941 AAGTTTTATT ATCTGTGGCT GGTTGAACAT AAATACACCC ATGGATCCTC GCGAAGGAAC
24001 AGTGCCGCAA TATTTCCCAT GTTATTAATG ATTGAAACAT CATTAGTAAA TGATTCACAT
24061 ATAGTATGCC ATACTCCTGT GTTATCTTTC CAATCTAATA CTATGTTAGT ATCAAGTTTG
24121 AATTCAGCAT CATCTGATTC ATAATCATAA TTTATACCAA CTCCAATTTC TGATTTTCTA
24181 GGAATTTTTT CCTTGGTTCT TAGATGCATT AACACTCTAA AATATTCGGC ATTTTTAAGA
24241 TCGATGGAAA TAATAAAATC CAAAGTTCCA TAATGAAAAA CTTCTTCTTC TTTTCCAAGC
24301 ATTTCATCAT GTCTATCATA ATCAAATAAA ATAACCGTTT CATCTTCTAC CATCGATAAC
24361 AGGTATTTAA CCTCATCATT ATATATATTG CCTTTTGAAA AATTAATTTC CATTGAAGGA
24421 TTGAACGTTA AATTAATATG ACCATTTCCT GGTGATATAT ACGAGAGATC AAAAATATTT
24481 CCGGTAAAAC TGGCTAATTT ATTTTTTGTG GTTATAGATT CCTTATATTC GGCCAAATAA
24541 TCTGTAGCAA ATTGATTGTT GACTTTGTAT TCTGTCCTGG TATCAAGTTC TGATAATGTG
24601 CTTTTAACAA TGGCGTCTAA ATCATTTTCT GTGAGAATGG ATAATGTCAT ATCAGGGTTA
24661 ATGGTCATCC CTTCTCTTGC AGGAAGACTA TTAAAAGAAT AATTGTCTTT TTTCTCATGG
24721 AAATAAACAA TAATGACGTC TTTTTCATAA TCACAAGAAC AATACATACC AATGCTGGCT
24781 TTTTTATTGA TCAGGTTTTC TATTTTATCA GTCACATTAA AATTAAACGG TGAGCTCCAG
24841 CTGCCATCAT AACGAATATG TGACAGTTTT AATATATAAT CAGTGATATC TATCTTGCCA
24901 TCTTCACTTT CATTTTTCAG CTCTTTTTGT TCCAGCCACA GTAAATACAA ACGAGACTTG
24961 TAAATAACAG GTCTGATATT TTCCTGCCAT ACATTGATGG GTATTTCAAT TTTTTTCCAT
25021 TCTCCCCAGG CATTGGCAGC AAATTGACCG TGCTGGCACT TTTGGTGATC GACATTGCGC
25081 CAATAATATA TTCTGGGTTC TGTCTGGCTA TAACCAATTA AATAAGTGAG CCCCTCATTG
25141 ACATTAATAC TGTCATGATA TCCGCTAATC ACCTGCAAGT TAGCGACATC TTCAAATGCG
25201 GTCAGATAAT TTTTAAAGCT ATCTTCAACG GTATCGATAT TTAACTGACT TTGGGAAAGT
25261 TGCTGTAACA GGTTGTTCAT CATACCTGTC TGACCAATAC GAATCGTGGG GTCGATATAG
25321 TTTTCCGGAT AATAGGCCAG TTCAGATACG CCGGCCCAGG TGCTATACCG TCGATTGTAG
25381 GTTTCCCAGT CGCAGAAGAA CTGACGGGTT TTCACTGGCT TTGATACTTT TCCTTCAACA
25441 TTATTCAACG CCCGGTTGAC ATATAACTGA ATGCTGGCAA TGGCTTCTGC CACACGGGTG
25501 GTTTTCACTT GGGCAGAAAC TTGGTTATCA ATCAGCAGAT AGCTGTACAA CTCATCCCGG
25561 CTCTTAATCT GTTGAGGTGC ACCATTTTTG ATGTAGTAAG CACTGGCCGC TGTCGTCGTG
25621 GCTTCATCCA GCCATGCCTG AAGCTGGTCG GATTGTTGAC TGTTCAGTCC CGCCTGCAAC
25681 AAAGTACTGG CGGCTTGCCA ATCATCAAAT GTTGGCATCG GGGTTTCCGG TTCACCGACA
25741 TATTTTAATT TTATGAGTGC AGCAACACCA TCCGGGGTAA TACCCAATGT AGCAGCGACA
25801 TCCAGCCATT GCAGAGTGAC ATCTATAAGT TCTCCAGTTG GTAAAGGTAT TCACTCCCAA
25861 ACCGGTCTGT TGCAATGCTT GTGTCACAAC CTGAGCATCA AAATTTTAAC GCCACCGCCA
25921 AATTGTTCGG CAGTCAACGC TCCTAAGTTC CAAATGCTGT TAAGATTCTG TCGCGTAGCT
25981 TCACAACGCA TGATCACAGC ATGGAAGCGG GTCAGCGCTT GCAAAGTGGG GAGATCATGT
26041 TGCAGTGCTG TGGTTTCTGA TTGGAATTTC TCCGGTTTTG TCACCAACAG GGTCAGTTCG
26101 TTTTCGCTGA GTCCAATATT GCGCACAATC AGAGAAAGTT GCCCCAGTAC CTGACAAAAA
26161 GCCACCATGT TGCTGGTTTC ATTCTCTGAG CGATCACGGT TAGCCGCAAT AATCATGAAA
26221 TCATCGAATG TCAGTCCTTG TGGTTTTATC TGATTAATCC ACAGCAAAAT AGTTTCTGCT
26281 GTTTTGGCTG AATCCATTTG AATGCTGGCA GCAATCAGCG GGGCAGCTGC ACGGATCAGT
26341 TCGTCATCAC CGAGTGAAAG TGTTGATAAT CCATTACTTA GTGTCGTGAT AAGGTTTTCA
26401 ATATCCGGCG TAAGGACAGT GCTGTAATTA TCCGTGGTCA TCAGAAACAC ATCACTGACA
26461 GACCATTTCT GTGTTGTCAG CCACTGGGTG CATTGGAACA GAAAGCTGAT TAATTGCGTT
26521 AATGCTGTAT CAGAAAAAAG GGCAATTTTC GTGTTCACAT AGGGAGAAAC CGACAACAAC

BNSDOCID: <WO___9808388A1TI_>

Fig.2.

26581 ATGGATAATT CATTCACTGT CAGATGATGA ATGTCTGCCA GCAGACGAAC GCGATAAAGC
26641 AGAGACAGGT TCTCGATGGA ACACATAAAT TCTGGATTTG TTCCGCCATT AGCCAGTTTC
26701 CATAATGTAT ACAGTTCAGT ATCATTCACT CTGAAAGCAC GTTTCATTAT TCCCAAATAA
26761 AAATGGTTTT TTGATTCACC GGGGGTTAAA TCCAGTTTGG TATTATCAGC AGAAAACTCT
26821 TGGCCATTTA ATAGCGGTGT ATTGAACAGC ATTGTAAAAT GACTGGGTTG TTGTTTAGTG
26881 GAATATTGGC TGATATCTGA ATGACACAAT ACCAGCGCAT CGCTGACGCT AATATTATAG
26941 TGCTGCATAT AATATTGAAC ATAAAACAGC TTACCCAACA CATTGCTGTC AATGGTTAAG
27001 TCATCATAAA TACTTTCTAT TACTTGCCAG ATATCTTCTG GAGATATGCC TGTGGCTTTA
27061 TACAAACGAA TCGCTTTATT CAGCTTTAAC AGGAATATAT CACCGGGAAC TCCATCATTT
27121 TAAAGTGTGC ATTGGCATTG ATAGCATCCG ACGGATTTGG TTAACTCGCC ATAAGCGGAG
27181 TGTTATACCG TTGGTGATTT GCTCTGTCGT CAATTTAATG GGAATACTGT AATGGGTATT
27241 AGCAATGGGG ACGAAATTTT TATCTTGGTA TATATATTCT TTATCTCCAT TCTGGAGACG
27301 AAAATCCAAG TGGTCAGGTT CTGTTTTTTT TACACTGAAA TTATATTTGT ATTCATTTTC
27361 TTTGATTGGA ATTAGCTCTG CATAGTTTAA ATGTGAATCG TAGAAATCTT TGCGGGTTCG
27421 CTTAATCAAT CTTGCCGTTG CCGTATCATT CCCGTCATTG ACCAATGTTA TCAGTTGCTC
27481 ATTCTTATAC TGTTGATTTG TATTTTTCTT ACCGAAGGAG AGATTGACAA ATAAACTGAG
27541 TTCATCATAA GACAAATCGT AGTAGCGAGC CAAAGAAGCA TAACTCTTAA AAATCAGTAC
27601 ATCATCTGTA CCGAAATTTT TCTTCATCAG TTCTGTTGAA TTTTCCGGTG TAATTTCTTC
27661 TACAAGGATT TGATACAATT CAGGCGATAT ATCAGTCTTA ATAGCCAGTA GCGATGTTGG
27721 GTCCATTAAT TCCGCTACGT CTGTATTACG GCTAAATGCG GTGAGGTTTT TATCTTGCAA
27781 TAAAATTGCC TGACGGGCTG ACTCATACGG CAGATGATAG GGTGTCATGC CGGTTTGCCG
27841 GTAAGTGGAC AACATTTTCA TTACACCGTT ATAGTCAGTT TTCTCTAACG TCTGAATATT
27901 ATGCAGCAGT AATTCATTAG ATAAGGATAA TGTGGAAATT TCTTCATCCA TATTATTCTG
27961 TGTCAGTGCC AGTGAAGCAA TGTCGGGGCG TCGTTTATTC AGGTGATATT GAGAATTGTC
28021 AGGATGAAAA TCTTTCGCTT CCCGATATAA TTCTGTTAAA TAAGCCGCTG GTGAAAATAT
28081 GGAAGCAATT GATCCCGGTT TTACAAAACG GTGGGCGCGG CCATAAAACC AACTGTTGTA
28141 ACTATTGTTT AGGGTTGACG GTGTAATATT AAGGTTAGTG ATATTAGCCA GTTGTGGATT
28201 AGCACGGGAC AAAATGCGCA GTTCTTCAAG TTTATTCTGT TTTGATTCCT GATGAGCCTG
28261 TTGATATAAA AAGTCTGTTT CTCGCCACGT CAGAGTTCCA CTTGTCCTAT GACGAAATTC
28321 GCTGAAAGAC ATAAACGAAA TGTTTGTCAA TAATAAAGTA TCACCAGCCT TTTTCTATTT
28381 ATCTTATCTA ACAGTTCATT AACTTTTATC ATATAAATCC TTAAGTTATT GTCAATTTAA
28441 TGATTAATGG TTTTTAGGTG GAGATTATTA TAATCTGATA GGAATATTAT GGTTAATTAA
28501 ATTGATACTG ATTTATCGCT CTATTCTTTC AATAAAAAAT AAAGAACTTC CCTATAATAC
28561 ATGGATTTAA ATAATGAATA CCGTATGTTA AAAATTAAAT TTTAACAAAC TTTCATGAAA
28621 AAATTCAACT CAACAATTGT TTAAATATTT TTAATTGTGT TTGTGCTGTT TGAAAAATGA
28681 ATGACTAATA TTTATCTATG AAAGATTATT TATTGAGGAT GTCTTGCTTG GTTTCAGGGG
28741 GCTACGTTGG AGTCAGATAA ATGTGTGCAA AAAGAAATCC TTAATAAAGT TGCGTAATTA
28801 CAAAAGTTGG TATATCGTGA CAAGAGTGAT AGTAATGTCA CATAATTTAT TGAATACCCG
28861 AACCTCGCAA ATGCGGGGTT TTTCTTCGCA TAATCAAAGA GAAAGCTATG AAAAAAACAC
28921 TGATTACTCT TATTCTCAGT ACCCTTTCTT TTGGTGCTTT GGCACAGCAG GGTGGCTTCG
28981 TTTCCCCGGA CAGCACAGAC TATACTCAGG GTGGATTTAA AGGTCCAACT CCCAACCTGA
29041 CCAGCGTTGC TCAAGCAAAA TCTTTTCGTG ATGATGCGTG GGTTGTTCTG GAAGGAAACA
29101 TTGTTAAACA GGTTGGTCAC GAACTCTATG AATTCGCGGC CGCATAATAC GACTCACTAT
29161 AGGGATCGCT TATTACGGAC TTATCCGGAA AGCTATCTGG AACCCCTGTT ACGCCTGAAT
29221 AAAACAGAAT TCAGGGATAA CAGTGGTTCT GTTTATGTTG ACATTGATGA TAAGCGCTGG
29281 ATGGGTCTGA CGGCCACTCC AACTGACAAA GTTCGTATCG AAGGTGAAGT GGACAAAGAC
29341 TGGAACAGTG TTGAAATTGA TGTCAAAACT ATCCGCATAG TGAAATAACT CAAGCACTTT
29401 GAATATAGCC CCGCACTCGC GGGGTTTTTT GCTTTCTGGG AGTCGGAAGT TTAACCGTAG
29461 TGACGAGGAT CAAAACTAAG TTAACGGCAG TGGTCACTGA TTTGGTGCAT AAGTTATCAA
29521 AAGTTAAAAA TCAAAACTTA TTTTTTATTT AATAGAGGAA TGTCACCCTG TAGGTGAATA
29581 ACGTTGACGG ATGTAAATAT ACAGTATTAT AGTCCTTTGA TATGTTATTA AATTGAAAAA
29641 CCTTTAAACT ATATTCGGGG GAAATTATTA TGTCAGATGT TCGTAATATT ATTAATGTTG
29701 ATAACAATTT TGGTTGTGAA TATAAAGCGG ATTTATTTAA ATAAGTTTTC ATAATTGTGA
29761 TACACCCATT TTTCTCATCC CCGGTTTTTG CTGTTGTAAG GAAGCGGTTT CCATGAAGAT
29821 TTTGACATGG TTAAGCAACT GCCACATAAA TTGGCAGCAG TGGTTTCGTG TCACGGTTTC
29881 ATGCAAGGAT TGCCATAGAC GTTCAATTTT ATTCAACCAC GGGCAATAGG TCGGTAAAAA
29941 GAGAAGATTA AATTTGGGAT TCTTTGCCAG CCAAACCCTG ACCTTCCGGC TCTTATGAAT
30001 GCAATAGTTA TCTAAAATTA ACGTGATGGT TTGGCATTA ACATATTGAT TGTTAATTTC
30061 ATCTAACAAT TTGATAAATA AATCTGAGTT CTTTCTCAAG CTACCGACAT AAGTGATTTC
30121 TTTCGTTTTC GCGTTGAGGC AATTGGCAAG GTAGTGTTTT TGGTTCTTTC CGGGGGTAAC
30181 AACACGCTTT TGTTGCCCTT TGAAGCACCA GTCTGCACCG ATTTTCGGGT TCAGGTTGAT
30241 GTCCACCTCA TCCTCATAGA AGACCGGGTG TTTCTCTTGA GGCATTGGAT AACGTCTCGC
30301 TGATTTTTGC CATTTTTTCA TCATACTCAG GGTCAGGCAA TTTTACGGTT GGTGCCGCCC
30361 TTCGCCAAAC GATGCCCGTC CGGCAAAAGT AGCGATAGAG GGTACTTTGA GAGAGCGATG

SDOCID: <WO_ 9808388A1TI_>

Fig.2.

30421	TATTCAGTAG	CTCATTGATT	TTAAGTGTAA	TAAGCTCAAG	GCTCCATCGT	GAACGGAGAT
30481	AGCCAAAATG	TTGTGGCGAG	TGCTGTAATA	AGAAAGAAAT	GACTGTGAAG	AGCGGAGCTA
30541	AGTTCCAGAT	GGCAGGCCTT	CCCGCCGGGA	GGCTTTTAAG	TCCTTCCAAC	CCGTATAATG
30601	TTAACCAATT	TACCCAACGA	TGAACGGAAG	AACGTGAACA	GTGAAGCGTT	CTGGAAACGT
30661	GAGAAACCGT	ACTCCCTTCA	TGTAACATCA	AGAGCGCGGT	GAAGCGACGT	GCATAGTCCT
30721	TATCCCGGGT	TTTCTGGATA	GCTTTTTTCA	TCGGACGTCG	TTCATTTCGG	GGTATTGATG
30781	TTATGATTGG	CATGACTCAG	TCCATTTTGG	GATTTGTTTT	GATTTGGCGA	TTAATCAGAT
30841	CGCGAAAATC	GGACTGAGTT	CCCTTCAAGT	GATCTACTAT	TTTGAAATCT	TATTTAATCA
30901	GGAGTCAGCA	AATGAGTTAT	TCCCCATAAT	ACCTGACCAT	GTGGTTGTTT	ATCCGGGAAA
30961	TGATTCATCT	ACCGGTGGTA	TGTGGATTCC	TTGGTGCGAT	AGTCAGAAAG	ATATTGACTC
31021	TGGCCATTAT	ATCAAAGTTA	CTTTCAGTAA	AAAGGACGCT	GCTGATATTG	TGAACTACAT
31081	GTTTCAACAT	GGCAGTTATG	TTTATTTTAC	AGACAGTAGT	AAACAATTTA	GCAATAAGCA
31141	AATTATGTCT	GGTGATTCAG	CTAAAGGCAA	AGGGGATTAT	AAGCTTGAAA	TTAAAACAAA
31201	CGGGAACCTT	CCACTGATGG	TATTGAATAA	ATATTGATTC	ATTATTATTT	ATGGATAAGA
31261	AATTAAGTTT	ATATTTCATC	TGGTTTCTGC	AATTAAGTTT	TAAAAATTAA	TTCTACTTTT
31321	TTTATGGTTT	TATATTTAAT	GCCAATCATA	TTATTTTTCT	TATAATAATT	GATAGTTTAT
31381	TTATATAGTA	AATAAATTCT	GTTGGATGTG	ATTATTATTG	TGAGACGGTA	ATAATTAACA
31441	TAACAGAAAA	TTCATGGTTA	GGAAATTCAA	TCAACTTTTG	TCCGGTTTCC	TGACCATGAA
31501	GAGCTGTATT	TACTGTAGAA	CTCGCATTGA	TACTGGATTG	ATTAGCCGGA	CGAGTGTTGG
31561	GTCAGCAGAT	AATATGTTGT	ATATTGGCTG	TGGATTTTTC	AGCGAGATGA	TAGCTTTGGC
31621	AGTAAAGGCG	ATTAATAACC	GATAAAACAG	AGAGACGGAT	TGTGGCCAGG	AAAGCAAAAA
31681	AGCCTCACCA	TGACGCGTTA	TTCAAACATT	TTTTAACCCA	ACCAGAAACC	GCCCGGGAAT
31741	TTTTATCCCT	TTATCTGCCG	GAAGCGATCC	GGTCAGTGTG	TGATTTACCA	CACTAAAACT
31801	GGAACCGGCA	GCTTTGTGGA	CAGGCAATTA	CGTCAGTTGC	ACAGTGATGT	GCTGTATTCT
31861	GTCGAGACAA	CCCACGGGGA	CGGTTACATT	TATTCCCTGA	TTGAACACCA	GTCCACGCCT
31921	GATCCGTTAA	TGGCCTGGCG	GCTGATGTAT	TATTCGCTGT	CAGCCATGGC	TGCGCATCTG
31981	AAAAAAGGAC	ATACTGAACT	CCCTTTGGTC	GTCCCCCTGC	TGTTTTATCA	TGGTGAGGTG
32041	AGGCCTTACC	CTTACTCAAA	TCGATGGCTG	GATTGTTTTA	CACTCTCTGA	ACACGCGGCT
32101	CACCTGTATA	ATCAGCCCCT	GCCGTTGGTG	GATATCAGTG	CGCTCAGTGA	TGAAGAGATC
32161	CTGACACATA	AAAGCATTGC	CTTGATGGAG	CTGGTACAAA	AACATATCCG	TTGCCGGGAT
32221	ATGCTGGAGT	GGGTTCCCCA	ATTGGTGGCG	TTGTTGAATG	CCGGTTATAA	TAGCGCCGAA
32281	CAGCGCCATG	TTGTGTTAAG	CTATATTTTA	CTGAATGGAC	ATACGCTGGA	TCTCGCCCAG
32341	TTTGTCCATC	AACTGACTGA	ACAATCTCCG	GAGCATGAAA	CCATGTTGAT	GACTATTGCA
32401	GAACAGCTTG	AACAAAAAGG	GCGTGAGCAA	GGCCGGACAG	AAGGCAGAAC	AGAAGGCAGA
32461	GCTGAAGGAC	GGGAAGAAGG	CAAGCTGGAA	ACGGCGCGCG	CATTATTACG	GCATGGTGTC
32521	AGTCTGGACA	TCATTGTCAC	CAGTACCGGC	CTGACCCGGG	AGAAAATTGA	AGCGTTAAAG
32581	CATTAAATGG	ATACGCTTTT	TCACAGCAGG	ATATGGTGAC	CCCTGTGAGG	CCACCGGAAA
32641	ATTTTATTTA	CTACGATTTA	CGACGGGTTA	CTTTAGGAAG	CTGAATGAGA	CGTCCTTTGT
32701	TATATAACGG	TCCCATATCA	ATCTTCTCTT	TTCCGCGTAC	AGGTAAGTAA	CCCAAACCTT
32761	CGTGAGCAGC	ATTTGCCAAC	AGGCCATCAT	CCTGATCGCC	TGACCAAGAG	AAGATCCCGC
32821	CCAATTTCAT	TTTGGTTGCA	TAAATTCCCT	TATGCAGCAC	AGTGCGGGGC	GTATCCAGTG
32881	AAATCCAGTG	ACCACCGTCA	GCATTAAAGA	GTGCGTCAGC	GTCGGTTTCC	GTGTCTGTCA
32941	CCAGTTCAAA	CTGATTTTTC	CCGCGTGCAA	TTTCATATTC	CGCATCGTAT	TGGTTATTCA
33001	GCAGACAGAA	GAATTCCGGA	GCACCTTTTT	CCATCGTGCC	CAGTGGCTCT	CCTGTTCTGT
33061	TATAGCGGCG	CGTTGTCAGA	TCAGCACCCA	GACATGAACG	TCCATAGTTA	GCAAATCCGA
33121	GGTGAATTTT	CTCCGGTTGT	ACACCTTGTG	ACAGTAAAAA	GCGGATCGCC	TCATCTGCCG
33181	AGTAATCCAT	GTCCCGATCA	GGATTGGGCG	GAGGAGGCTT	ATCGCCGTCA	TATTCATATC
33241	TGGGGGGATA	CAGGTTAGTA	TGGTGACCGA	TGTATTCTGC	CCAACCGGTA	CCAAAGAAGT
33301	CGTAGGTCAT	CACAAAGATA	TTGTCTAAAT	AAGGTGCGAT	TTCTTTGAAG	CTGGACTTCT
33361	CCATTTTGGC	AACGACGGCG	CTACAGGCTA	TCGTGATTTC	TTTACGGGCC	CGGGTTCCAA
33421	AGGCGATGTT	CAGTGCTTCA	CGCAGCTCTT	TCACTAACAA	AACATAGTTT	GGGCCATCAT
33481	GTTCCGGGTC	GAATTCATTA	CCTTCTTCAC	CTGTGGCGCC	GGGGTATTCC	CAGTCGATAT
33541	CCACCGCAGT	AAACATGGGA	AAACGCCGGG	AAGAAGTCGA	CGATGCTACT	CACAAATGTA
33601	GCACGTTGCT	CAGGATCTTT	GGCCATCACA	GAGAAATACC	CTGACATACT	CCAGCCGCCG
33661	ATACTGAATG	CGAGTTCCAG	CTTATGCCCT	GCCTGTTTTG	CTCGCGCTTT	CAGATTACGC
33721	AATCCCCCCA	GTAAACCGGA	GGCTGCATCC	TGATTGTAAT	ATTGCAAGAA	ATTCTTCGGG
33781	CTGGCATCAC	GGCGCTGATC	CGCGTCCAGA	CCGACATTGC	GTGTGGTGCC	TAAATCACCA
33841	TAAGGATCAA	CGGGTACAAT	ATGGCCTAAT	GTAATAGGGG	CAATCTGGCC	ACTGCTGGCT
33901	TCTGCTTGCC	GGTTCCACCC	GTCAACAACC	TCATTAATCC	GTTCGGATAA	CTTGCCTTTG
33961	TCACCGTTGA	CGGCCATAAA	ACTGAAAATC	AGGCGGTCGT	AGGCGGTAGG	CGGGATTTTT
34021	TCCAGATCAA	AACCACGGCC	GGGGGCATCG	TCGCTGGTCA	GCGCAGTGTT	ATCCTGGGTT
34081	TCTGGCGACA	AACGCGCATC	ATACTGGCAC	CAGTCAGTAA	TATAGGCAGA	GACTTTAGGC
34141	AGCGGTTCTG	TATTTTCCGG	ATCAACTTCA	TATTCGTTGT	ACAGGGACTT	GGCAACACGT
34201	GCTGAAGAAT	AACTCAAAGG	AGTTCCGCTG	CCGTCAGGTT	TATATCCCAC	CTTCTGATAG

BNSDOCID: <WO_ _ 9808388A1TI_>

Fig.2.

34261	GTTTCTTCTG	TGAGTGCATC	ATATTGCAAT	ACCTCGGTTT	TTTCTCCCGG	CGGTACATCA
34321	GGCGTATTGG	GGTTACCGTG	ATCGGCAATT	TCTTCCGGTG	TCGCCTCACG	GACATATTGC
34381	CAGGCATTCT	CATAAACCGG	TAAATCAGGT	GAAATATTGC	GGTCGGGAAT	ATGCCAGCGT
34441	TCAACCCAGC	CGATGTTTTT	AAAAACCGCG	CTATCATAAA	TGACATACCA	GGTTTGACCA
34501	CCAGATTGAT	TCTGCCAGGC	AACCAGAGAT	GCGCCTACTT	CGCTGCTGGC	GTCAGACATC
34561	GCTTTAATTG	AAGGGTATCG	ATAAACATTT	TGAGACATAA	TTTCACTTCC	GGCCCCGTTA
34621	TATTCCGGGG	CCGGCTCCTG	ATATCAGTTA	GAATTGTCTT	GTTTTAATTG	ATGTTTATTC
34681	AGACGGCTAC	GAACCTGCTG	GCTGAACTCA	TTACTTCCGC	CACTCACATC	ACGCGCGGTA
34741	TAACGCAGAT	GGAGGATAAT	ATCGCTCAGC	GACTCCAGCA	GCTGATCCTG	ATCGGAACCG
34801	AATTCCAACT	TCCACTGTGA	AATGGCGCCT	GTCCCTTCAA	AAGGCAGGAA	AAGTTCATCA
34861	TCAAAATTGA	GCCTGAACAT	GCCGCTGTCT	TCCATGGCCG	TTGAAATCAC	CACACCTTGA
34921	TTAGCCTGTA	CGTTCAGCAA	AACGTTTTCG	GGTTTGGTGT	ATTCCAAGGG	GTTAAGCAAA
34981	TAATCGATAG	TTTTTAAGTC	AGCAGTACTG	TAAAGCGTAT	TGCTGAGTTG	TACCAGTGAA
35041	GCCCGTACAT	CTTCATAAGG	CCCCAGCAAT	GCGGGCAATG	ACAGCGCTAC	GGTTTTTATA
35101	CGCCGATCAG	CGTGGGTCGG	ATAATCGCGC	AAGAACATTT	CGGCGCTCAG	TAAGAAAGTG
35161	AATGAACCCG	TACTCTTGCC	AATTTCCCAC	TGTGATGATG	TCAGTAATGA	TTTTACCGAT
35221	ATGGTTTTTA	TGATCTCCAG	ACGTCTGGTG	TTATGTTGCA	AATACGCCTG	ATCCATCCGT
35281	TGTAAGGCTA	ATTTCAGATG	TTCTCCGACC	AGCAGCCCCT	GATAAAGATC	ATTCCAGAGA
35341	CCACTTTGGA	CGAAATTCAT	ATCATACTGA	CCTGTTTCGT	ACTGCCAGGA	GGCTTCGGCC
35401	AGTAAACAGA	GGGAATTAAC	CGCATCATAG	GCTTGCAGGT	AAAGCCGGAG	ATTTGGCTGA
35461	TCATTCACAT	GTATAACGCA	TCATTGGTAN	ANTTGTTCNN	NNNNNNNNNN	NNNNNNNNNC
35521	CCGAAGCATA	CCGCCAAGAC	CATCCCCCCG	ACGGCCAGAC	CGAAAATATT	GGGAACCATA
35581	TCCGCCACAG	CGGCCGCAGT	GGCGGCTGAC	TGGGCAGCGA	TCACACCTTC	AGCCGCTCTT
35641	GATTGTAATG	CGATAACTTC	CTGCTCGCTG	ATGGAGATGT	TTTCATCATA	GAGCGATTTA
35701	TAGTGTTGCT	GGCGCTCCTG	AGCGGCCCGT	CGGCTGATGG	TCAGTGCATC	CAATGAAGCC
35761	TGTTGCATGT	CAATCGCTTG	CTGTTGCAGA	TTGCGGGTAA	AGCTGTACAG	CCCCAGTTGC
35821	TGCTGCATAC	GGAAGTGTTC	AAAATCGGTA	TTGTCTTTTT	TCTCCAGCAA	ACTCAGTAAC
35881	GTGCTGCCGT	ACTGAATCAG	CGTTTCTGCG	GCCTCTTTTG	CCCGGCTCAT	GATCGGGGTG
35941	AAACGATAAT	TCGGGATTGC	CCGGCGTTTC	ATGCCCGCCA	TACGATTAGC	CACAACACGC
36001	TGGTAACGCT	GCCTGAGCAG	ATCTTGCGGG	CTGATGGGTT	CATCGTATAA	TCCGGCCGGA
36061	AACTCTTTAC	CATCCAAGGT	CAGGTTATGA	CGTAAGTTAT	ATAGACGCTG	ATCCAACATT
36121	TGCCACAGTT	TGAGATATTC	CGTATCAACA	GGTTTGACAA	ATAAATCAGA	CGGTGCGGCA
36181	GAGACGGATG	TATCATATGT	CACAGGCAGA	AGTGGCACGT	TGCTGACAGT	AAGCATTAAC
36241	TCCTGTGCCC	GTGCTTCACT	GTTTTCATAC	AGAGCCACAT	CTTGCAGCGT	ACGGGGTTGC
36301	CAGTTTGCCG	CGAGCAGAAT	ATCAGGGCTG	GTACCCAGTA	ACATATTGAC	GGAGTCATAG
36361	ATCTGCTTGG	CGACAGTACG	TGCACTGGAT	GTCAGCTTAC	GGTATTCCAT	GTCTCCCTGA
36421	TCTAACAGAT	TCTTGACATA	GAAACGGAAT	ATTGCTTTCC	GGTAGTGAAT	GGGTTCACTG
36481	GCTGCAATGG	CATCCGGATC	GGTTGGTTCA	ATTAACATCC	GGTACACGGT	GGGTGGAGGA
36541	TCAATAATTG	GCCGTGAATT	CCAGTAACGC	GGTTTACCTT	GGTTGCTGGC	CTGAACAAGT
36601	TCATCTTCCA	GCGGATTAAA	AATATAGTGC	AGCCATTCGG	TGGCCTCTTT	TAATCGTTGT
36661	TCTATATTCA	GTCGCCACGC	GACCAGAAAT	GGCATATGGA	AAAACAGTTC	CCAGAAATAG
36721	ATCCCATTTG	CGCCATTTAA	ATCAATCGGC	GTAGGGAATG	AACCGGGTAT	AGGCTGTTCG
36781	GTAATAAGCT	GTGTATTCCA	GCTCAGTACC	TGCGGGATAC	CCTGACTGGC	AATGGCGATC
36841	AGTTTTTTTG	CAAACAGTGT	ATTAAGGCGA	ATGTTTTGTG	GCGCGTTATC	AGTTTCATCT
36901	GCGGGGAAGG	AAAGGAATTG	CACCTGATCC	TGTTCATTGA	GTTTAATCAG	TTCGCGAATA
36961	TGCATACCGA	TTCTGAACTC	TTGAGTACAG	CTGGCACTTT	CATTGCCAAC	ACCACCTTTG
37021	GGCTTAAAGA	GAAGTTCGGC	TTTCAGGGTG	ATTCGATTAT	CCGACCCCAG	CTTGATTGAT
37081	GGATAGGTTA	AATCAAGAAC	TTTTTCGCTC	AGTACCAGTG	GTTGTTCATC	CAAGACAGTA
37141	TTATCGTGCA	TCAGCCGGAA	AGAACCGTTG	TAATATTGAT	GATCTTCTAT	CGCACCAAAC
37201	TTAAAGTCAG	ATTGAGCGAC	AATCTCCAGT	GTGTCATCAG	TGCCATGAAC	AAAATTGACA
37261	ATCAGTTTGA	TACTGTCTTT	GCCGAAATCA	GGGTTCATTC	CGGTTTGGAT	TCTCCGGCAA
37321	TAGGAAAGCG	TTCTTCCCGG	GTTGCCGGAT	AGAGCACCAT	AGTACGGTAA	TCGATAGGAT
37381	TGCCTTAAGG	CATCCTTGTG	TTCACGTGAG	TAATACCAGA	CCAGGTTGCC	GACATATTTT
37441	CCTTTTCGTC	CATCAGCATA	TTGGTCATCC	GGCAAATCAG	TAATTTCTAC	CAGCAGTGTA
37501	TCGCAGACAT	AACCGAAGGC	TTCGTCATAA	TCATAATCCT	TACCTTTCTT	ATCTGTCCCC
37561	TGAAGACGGA	CAAACGGAAC	CAGAGCCAGA	AACGGGTTAT	GCGGGTCTTG	CTGTATATCC
37621	ATCACAGCAA	CCATCTGGGC	CATCCGGTAT	TGCAGATGTC	TTCGCGCAGA	ATGGTGGGTG
37681	TACTCCAGCT	GCCATCATAT	TTGGCATAAG	CGATTTTGAT	CCGGTCAGGA	ACGGTGTGGG
37741	AGGAACCCAA	TCACCCGCAC	TAGGCTCAAC	GTTTTGGTTA	TGCAGTGATA	ACGCAGTTGT
37801	ATCTTTAGTT	TCAGACTGTT	CTTCAACTTC	CGTCCAGGCA	ATATACAGGC	GATTATTCAG
37861	GAAAATGGGG	CGTATCAAAT	TGGGGTCTAC	GCTGCCCAAT	GGCAGGTCAA	TAGGTTTCCA
37921	CTCGCTCCAG	GCATTGGGAG	ATAACGCATC	GGTATCAGGA	TGGCGTATCG	AAAGATTCAG
37981	TGAACGCCAG	TAATATTGGT	ATGGCTGTCT	ACGGGTACGT	CCGACAAAGA	AGAACTTATC
38041	GCGTTTGATG	TTAACACCAT	CTTCATAACC	TGCGATAACT	TTCAGGTTAC	TGACATCTTC

Fig.2.

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38101  AAAATTATTC AGATAACCGA GCACCGCTTG TTGTACAGAA TCTTCGGTAA TTTTTCCCTG
38161  ATTAAGGGCA CTTTCCAGTT GGAAGAAGAA TTCTGTTTTA TTCAGGCGTA ACAGGGGTTC
38221  CAGATAGCTT TCCGGATAAG TCCGTAATAA GCGATCCC
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N=unspecified base

Fig.3.